Current Clinical Strategies

Critical Care Medicine

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Contents

Critical Care Patient Management

Matt Brenner, M.D.

Critical Care History and Physical Examination

Chief Complaint: Reason for admission and system failure responsible for admission.

History of Present Illness and Hospital Course Prior to Admission to Critical Care Unit:

Diagnostic Studies:

Prior Cardiac History: Angina (stable, unstable, change in frequency). History of myocardial infraction. History of heart failure; ejection fraction. Call for old EKG's, echocardiogram, stress tests, and catheterization studies.

Chest Pain Characteristics:

1. **Pain:** Quality of ischemic pain
2. **Onset:** With activity, awakening from sleep, relation to meals.
3. **Severity/Quality:** Pressure, tightness, sharp, pleuritic.
4. **Radiation:** Jaw, arm.
5. **Associated Symptoms:** Diaphoresis, dyspnea, back pain, GI symptoms.
6. **Duration** of episodes.
7. **Amelioration:** Nitroglycerin, oxygen, rest.
8. **Congestive Symptoms:** Orthopnea (number of pillows); paroxysmal nocturnal dyspnea, dyspnea on exertion.
9. **Peripheral Vascular Disease:** Claudication, transient ischemic attacks, cerebral vascular accidents, renal disease.
10. **Cardiac Risk Factors:** Elevated cholesterol or lipids, hypertension; smoking history, male, diabetes mellitus. Family history of atherosclerosis (MI, stroke, peripheral vascular disease - age of onset.) Prior myocardial infarction.

Past Medical History: Peptic ulcer disease, COPD. Corticosteroid use. Functional status prior to hospitalization.

Medications: Dosage and frequency. Use of sublingual nitrate.

Social History: Tobacco, alcohol consumption.

Allergies: Dye, aspirin, opiates.

Review of Systems:

Physical Examination

Vital Signs: T, P, R, BP, pulmonary capillary wedge pressure, cardiac output; inputs and outputs.

General: Mental status, Glasgow Coma Scale

HEENT: PERRLA, EOMI

Lungs: Inspection, percussion, palpation, auscultation

Cardiac: Regular rate and rhythm, cardiac rubs.

Cardiac murmurs: 1/6 faint; 2/6 clear ; 3/6 loud; 4/6 palpable; 5/6 heard with stethoscope off the chest; 6/6 heard without stethoscope.

Abdomen: Bowel sounds normoactive, soft-nontender.
Neuro: Deficits in strength, sensation.
Deep tendon reflexes: 0 - absent; 1 - diminished; 2 - normal; 3 - brisk; 4 - hyperactive clonus.
Motor Strength: 0 - no contractility; 1 - contractility but no joint motion; 2 - motion without gravity; 3 - barely against gravity; 4 - some resistance; 5 -motion against full resistance (normal).
Extremities: Cyanosis, clubbing, edema, peripheral pulses 2+.
Skin: Capillary refill and skin turgor.
Labs: CBC, PT/PTT; Chem 6, Chem 12, Mg, pH/pCO2/pO2.
CXR, EKG, other diagnostic studies.
Impression/Problem list: Discuss diagnosis and plan for each problem by system.
Neuro: List and discuss neurologic problems
Pulmonary: Ventilator management
GI: H2 blockers, nasogastric tubes.
GU/Electrolytes-fluid status: IV fluids, electrolyte therapy.
Heme: Blood or blood products
ID: Antibiotic therapy
Endocrine/Nutrition: Parenteral or enteral nutrition, diet.

Admission Check List:

1. **Call for old chart, EKG, and X-rays.**
2. **Stat labs** - CBC, Chem 7, INR, PTT, T&S, ABG, UA.
3. **Additional labs** - Toxicology screens and drug levels.
4. **Additional cultures** - Blood culture x 2, Urine and sputum culture before starting antibiotics.
5. **CXR, EKG**, additional diagnostic studies.
6. **Discuss Case** with resident, attending or fellow, and family.

Critical Care Progress Note

ICU Day Number:
Antibiotic Day Number:
Subjective: Patient is awake and alert
Objective: T max, T, P, R, BP, 24 hr input and output, pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output.
Lungs: Clear bilaterally
Cardiac: Regular rate and rhythm, no murmur, no rubs.
Abdomen: Bowel sounds normoactive, soft-nontender.
Neuro: No local deficits in strength, sensation.
Extremities: No cyanosis, clubbing, edema, peripheral pulses 2+.
Labs: WBC, CBC, ABG, Chem 7.
EKG:
CXR:
Impression/Plan: Give an overall impression, and then discuss impression and plan by organ system:
Fluids/Electrolytes:
Pulmonary:

Cardiovascular:
Infectious:
Endocrine:
Nutrition:

Fluids and Electrolytes

Maintenance Fluids Guidelines:
70 kg Male: D5 1/4 NS with 20 mEq KCl/liter at 125 mL/hr.
Specific Replacement Fluids for Specific Losses:
Gastric (nasogastric tube, emesis): D5 1/2 NS with 20 mEq/liter KCL.
Diarrhea: D5LR with 15 mEq/liter KCl. Provide approximately 1 liter of replacement for each 1 kg or 2.2 lb of body weight lost.
Bile: D5LR with 25 mEq/liter (1/2 amp) of HC03.
Pancreatic: D5LR with 50 mEq/liter (1 amp) HC03.

Blood Component Therapy

I. Estimation of Blood Volume:
A. Total blood volume (TBV in liters) = 7% of body weight in kilograms.
B. Male = 77 x body weight (kg) = TBV (mLs)
C. Female = 67 x body weight (kg) = TBV (mLs)
D. Plasma volume = TBV-(TBV x hematocrit)
II. Colloid Solution Therapy: Indicated for volume expansion.
A. Albumin (5% or 25%) is useful for hypovolemia and hypoproteinemia or to induce diuresis with furosemide in hypervolemic, hypoproteinemic patients.
B. Plasma protein fraction 5% (Plasmanate): Contains 130-160 mEq Na/L; indicated for volume expansion.
C. Hetastarch (Hespan): Synthetic colloid; 6% hetastarch in saline. Similar indications as for albumin.
D. Crystalloids Solutions: Normal saline, lactated Ringers solution; used for acute volume replacement. 3 cc crystalloid = 1 cc whole blood.
III. Red Blood Cell Transfusions for Acute Blood Loss:
A. Control hemorrhage and replace losses with crystalloids until packed red blood cells are available.
B. If crystalloids fail to produce hemodynamic stability after more than 2 liters have been administered, give packed red blood cells.
C. If volume replacement and hemostasis stabilize hemodynamic status, wait for formal type and cross match for blood. Otherwise, administer O negative, low titer blood or type specific (ABO matched), Rh compatible blood, which can be prepared in 10 minutes and is not crossed matched.
IV. Blood Transfusion in Acute Anemia: Blood transfusion is given when hemoglobin is <8.0 and hematocrit <24%, unless patient has symptoms such as chest pain, dyspnea, sepsis, mental status changes. Assess rate of fall in hemoglobin, absolute level of hemoglobin, active bleeding, underlying coagulopathy, preexisting coronary artery disease or

ischemia.

V. Blood Component Products

A. Packed Red Blood Cells (PRBC's). Each unit provides 250 cc of volume, and each unit should raise hemoglobin by 1 gm/dL and hematocrit by 3%. PRBC's are usually requested in two units increments.

B. Type and Screen. Blood is tested for A, B, and Rh antigens and antibodies to donor erythrocytes. If blood products are required the blood can be rapidly prepared by the blood bank.

C. Type and Cross Match. Sets aside specific units of packed donor red blood cells. If blood is expected to be needed on an urgent basis, type and cross should be requested.

D. Platelets. Indicated for bleeding if there is thrombocytopenia or thrombopathy in the setting of uncontrolled bleeding. Each unit of platelet concentrate should raise the platelet count by 5,000-10,000. Usually transfused 8-10 units at a time and this many units should increase the platelet count by 40-60,000.

E. Fresh Frozen Plasma (FFP). Used for active bleeding secondary to liver disease, warfarin overdose, dilutional coagulopathy (from multiple blood transfusions), disseminated intravascular coagulopathy, vitamin K and coagulation factor deficiencies. Requires ABO typing, but not cross matching.

1. Each unit contains all coagulation factors in normal concentration.
2. 4-6 units are usually required for therapeutic intervention, and the frequency of dosing depends on clinical response.

F. Cryoprecipitate

1. Indicated in patients with Hemophilia A, von Willebrand's disease, and any state of hypofibrinogenemia requiring replacement (DIC), or reversal of thrombolytic therapy.
2. Contains factor VIII, fibrinogen, and Von Willebrand factor.
3. The goal of therapy is to maintain the fibrinogen level above 100 mL/dL. This is usually achieved with 2-4 units/10 kg or 1-2 units/10 kg depending on whether the fibrinogen content in the precipitate is high or low, respectively.

Parenteral Nutrition

Central Parenteral Nutrition:

-Infuse 40-50 mL/h of amino acid-dextrose solution in the first 24h; increase daily by 40 mL/hr increments until providing 1.3-2 x basal energy requirement and 1.2-1.7 gm protein/kg/d (see formula page 117).

Standard Solution:

Amino acid sln (Aminosyn) 7-10%	500 mL
Dextrose 40-70%	500 mL
Sodium	35 mEq
Potassium	36 mEq
Chloride	35 mEq
Calcium	4.5 mEq
Phosphate	9 mMol

Magnesium	8.0 mEq
Acetate	82-104 mEq
Multi-Trace Element Formula	1 mL/d
Regular insulin (if indicated)	10-60 U/L
Multivitamin 12 (2 amp)	10 mL/d
Vitamin K (in solution, SQ, IM)	10 mg/week
Vitamin B12	1000 µg/week

Fat Emulsion:

Intralipid 20% 500 mL/d IVPB infused in parallel with standard solution at 1 mL/min x 15 min; if no adverse reactions, increase to 100 mL/hr. Serum triglyceride 6h after end of infusion (maintain <200 mg/dL).

Cyclic TPN: 12h night schedule; taper continuous infusion in morning by reducing rate to half original rate for 1 hour. Further reduce rate by half for an additional hour, then discontinue. Finger stick glucose q2-6h; Restart TPN in afternoon. Taper at beginning and end of cycle; Final rate of 185 mL/hr for 9-10h with 2h of taper at each end, for total of 2000 mL.

Peripheral Parenteral Supplementation:

-3% amino acid sln (ProCalamine) up to 3 L/d at 125 cc/h **OR**

-Combine 500 mL amino acid solution 7% or 10% (Aminosyn) and 500 mL 20% dextrose and electrolyte additive and infuse at up to 100 cc/hr in parallel with:

-Intralipid 10% or 20% at 1 mL/min for 15 min (test dose); if no adverse reactions, infuse 500 mL/d at up to 100 mL/hr.

-Draw blood 6h after end of infusion for triglyceride.

Special Medications:

-Cimetidine (Tagamet) 300 mg IV q6-8h or in TPN **OR**

-Ranitidine (Zantac) 50 mg IV q6-8h.

-Insulin sliding scale.

Labs:

Baseline: Draw labs below. CXR, plain film for tube placement

Daily Labs: SMA7, osmolality, CBC, cholesterol, triglyceride (6 h after end of infusion), urine glucose and specific gravity, phosphate, Mg, calcium.

Weekly Labs: Protein, iron, TIBC, transferrin, PT/PTT, zinc, copper, B12, Folate, 24h urine nitrogen and creatinine. Pre-albumin, retinol-binding protein, albumin, total protein, SGOT, SGPT, GGT, alkaline phosphatase, LDH, amylase, total bilirubin.

Enteral Nutrition

General Measures: Daily weights. Nasoduodenal feeding tube. Head of bed at 30 degrees while enteral feeding and 2 hours after completion. Record bowel movements.

Continuous Enteral Infusion: Initial enteral solution (Osmolite, Pulmocare, Jevity) 30 ml/hr. Measure residual volume q1h x 12h then tid; hold feeding for 1h if >100 ml. Increase rate by 25-50 ml/hr at 24 hr intervals as tolerated until final rate of 50-100 ml/hr (1 Cal/ml) as tolerated. 3 Tablespoons of protein powder (Promix) may be added to each 500 cc of solution. Flush tube with 100 cc water q8h.

Enteral Bolus Feeding: Give 50-100 ml of enteral solution (Osmolite,

Pulmocare, Jevity) q3h initially. Increase amount in 50 ml steps to max of 250-300 ml q3-4h; 30 kcal of nonprotein calories/d and 1.5 gm protein/kg/d. Before each feeding measure residual volume, and delay feeding by 1h if >100 ml. Flush tube with 100 cc of water after each bolus.

Special Medications:

-Metoclopramide (Reglan) 10-20 mg PO, IM, IV, or in J tube q6h.
-Cimetidine 300 mg PO tid-qid or 37.5-100 mg/h IV or 300 mg IV q6-8h **OR**
-Ranitidine 50 mg IV q6-8h or 150 mg in J-tube bid.

Symptomatic Medications:

-Loperamide (Imodium) 2-4 mg PO of in J-tube q6h, max 16 mg/d prn **OR**
-Diphenoxylate/atropine (Lomotil) 5-10 mL (2.5 mg/5 mLs) PO or in J-tube q4-6h prn, max 12 tabs/d **OR**
-Kaopectate 30 cc PO or in J-tube q8h.

Radiographic Evaluation of Common Interventions

Central Intravenous Lines:

Central venous catheters should be located well above the right atrium, and not in a neck vein. Rule out pneumothorax by checking that the lung markings extend completely to the rib cages on both sides. An upright, expiratory x-ray may be helpful. Examine for hydropericardium ("water bottle" sign, mediastinal widening).

Pulmonary artery catheters should be located centrally and posteriorly, and not more than 3-5 cm from midline.

Endotracheal Tubes: Verify that the tube is located 3 cm below the vocal cords and 2-4 cm above the carina; the tip of tube should be at the level of aortic arch.

Tracheostomy: Verify by chest x-ray that the tube is located half way between the stoma and the carina; the tube should be parallel to the long axis of the trachea. The tube should be approximately 2/3 of width of the trachea; the cuff should not cause bulging of the trachea walls. Check for subcutaneous air in the neck tissue and for mediastinal widening secondary to air leakage.

Nasogastric Tubes: Verify that the tube is in the stomach and not coiled in the esophagus or trachea. The tip of the tube should not be near gastroesophageal junction.

Chest Tubes: A chest tube for pneumothorax drainage should be superior, near the level of the third intercostal space. To drain a free flowing pleural effusion, the tube should be located inferior-posteriorly, at or about the level of the eighth intercostal space. Verify that the side port of the tube is within the chest.

Mechanical Ventilation: Obtain a chest x-ray to rule out pneumothorax, subcutaneous emphysema, pneumomediastinum or subpleural air cysts. Lung infiltrates may diminish or disappear because of increased aeration of the affected lung lobe.

Arterial Line Placement

Procedure:

1. Obtain a 20 gauge 1 1/2-2 inch catheter over needle assembly (Angiocath); arterial line setup (transducer, tubing and pressure bag containing heparinized saline), armboard, sterile dressing, lidocaine, 3 cc syringe, 25 gauge needle, 3-0 silk suture.
2. The radial artery is the most frequently used artery. Use the Allen test to verify patency of the radial and ulnar arteries. Place the extremity on an armboard with a gauze roll behind the wrist to maintain hyperextension.
3. Prep with providone-iodine and drape; infiltrate 1% lidocaine using a 25 gauge needle. Choose site where the artery appears most superficial and distal.
4. Palpate the artery with the left hand, and use other hand to advance the 20 gauge, catheter-over-needle assembly into the artery at a 30 degree angle to the skin. When a flash of blood is seen, hold the needle in place and advance the catheter into the artery; occlude the artery with manual pressure while the pressure tubing is connected.
5. Needle and guide-wire kits may also be used; Advance the guide-wire into the artery, and pass the catheter over the guide-wire.
6. Suture the catheter in place with 3-0 silk and apply dressing.

Central Venous Catheterization

Indications for Central Venus Catheter Cannulation: Monitoring of central venous pressures in shock or heart failure; management of fluid status; insertion of transvenous pacemaker; administration of total parenteral nutrition; administration of vesicants (chemotherapeutic agents).

Location: The internal jugular approach is contraindicated in patients with a carotid bruit, stenosis, or aneurysm. The subclavian approach has an increased risk in patients with emphysema or bullae. The external jugular or internal jugular approach may be preferable in patients with coagulopathy or thrombocytopenia. In patients with unilateral lung pathology or a chest tube already in place, preferential placement of the catheter on the side of predominant pathology or on the side with the chest tube is recommended.

Technique of Insertion of External Jugular Vein Catheter:

1. The external jugular vein extends from angle of mandible to behind the middle of clavicle where it joins with the subclavian vein. Place patient in Trendelenburg's position. Cleanse skin with Betadine-iodine solution, and using sterile technique, inject 1% lidocaine to produce a skin weal. Apply digital pressure to the external jugular vein above clavicle to distend vein.
2. With an 18-gauge thin wall needle, advance the needle into the vein. Then pass a J-guide wire through the needle; the wire should advance without resistance. Remove the needle, maintaining control over the guide wire at all times. Nick the skin with a No. 11 scalpel blade.
3. With guide wire in place, pass the central catheter over the wire and remove the guide wire after the catheter is in place. Cover the catheter hub with a finger to prevent air embolization.
4. Attach a syringe to the catheter hub and ensure that there is free back-flow

of dark venous blood. Attach the catheter to intravenous infusion.
5. Secure the catheter in place with 2-0 silk suture and tape. The catheter should be removed and changed within 3-4 days. Antibacterial coated catheters or "cuffs" are used in patients with limited access sites or risk for infection.
6. Obtain a CXR to confirm position and rule out pneumothorax.

Internal Jugular Vein Cannulation:

The internal jugular vein is positioned behind the sternocleidomastoid muscle lateral to the carotid artery. The catheter should be placed at a location at the upper confluence of the two bellies of sternocleidomastoid, at the level of cricoid cartilage.

1. Place the patient in Trendelenburg's position and turn the patient's head to the contralateral side.
2. Choose a location on the right or left. If all other factors are equal (symmetrical lung function, no chest tubes in place), the right side is preferred because of the direct path to the superior vena cava. Prepare the skin with Betadine solution using sterile technique and drape. Infiltrate the skin and deeper tissues with 1% lidocaine.
3. Palpate the carotid artery. Using a 22-gauge scout needle and syringe, direct the needle toward the nipple at a 30 degree angle to the neck. While aspirating, advance the needle until the vein is located and blood back flows into the syringe.
4. Remove the scout needle and advance an 18-gauge, thin wall catheter-over-needle with an attached syringe along the same path as the scout needle. When back flow of blood is noted into the syringe, advance the catheter into the vein. Remove the needle and confirm back flow of blood through the catheter and into the syringe. Remove the syringe, and use a finger to cover the catheter hub to prevent air embolization.
5. With the 16-gauge catheter in position, advance a 0.89 mm x 45 cm spring guide wire through the catheter. The guide wire should advance easily without resistance.
6. With the guide wire in position, remove the catheter and use a No. 11 scalpel blade to nick the skin.
7. Place the central vein catheter over the wire, holding the wire secure at all times. Pass the catheter into the vein, and suture the catheter with O silk suture, tape, and connect it to an IV infusion.
8. Obtain a CXR to rule out pneumothorax and confirm position of the catheter.

Subclavian Vein Cannulation:

The subclavian vein is located in the angle form by the medial 1/3 of the clavicle and the first rib.

1. Position the patient supine with a rolled towel located between the patient's scapulae, and turn the patient's head towards the contralateral side. Prepare the area with Betadine iodine solution, and using sterile technique, drape the area and infiltrate 1% lidocaine into the skin and tissues.
2. Advance the 16-gauge catheter-over-needle with syringe attached into a location inferior to the mid-point of the clavicle, until the clavicle bone and needle come in contact.
3. Slowly probe down with the needle until the needle slips under the clavicle,

and advance it slowly towards the vein until the catheter needle enters the vein, and a back flow of venous blood enters the syringe. Remove the syringe, and cover the catheter hub with a finger to prevent air embolization.

4. With the 16-gauge catheter in position, advance a 0.89 mm x 45 cm spring guide wire through the catheter. The guide wire should advance easily without resistance.
5. With the guide wire in position, remove the catheter and use a No. 11 scalpel blade to nick the skin.
6. Place the central line catheter over the wire, holding the wire secure at all times. Pass the catheter into the vein, and suture the catheter with 2-0 silk suture, tape, and connect to IV infusion.
7. Obtain a CXR to confirm position and rule out pneumothorax.

Pulmonary Artery Catheterization

I. Procedure

A. Using sterile technique, cannulate a vein using the technique above. The subclavian vein or internal jugular vein are commonly used.

B. Advance a guide wire through the cannula, then remove the cannula, but leave the guide wire in place. Keep the guide wire under control at all times. Nick the skin with a number 11 scalpel blade adjacent to the guide wire, and pass a number 8 French introducer over the wire into the vein. Connect the introducer to an IV fluid infusion, and suture with 2-0 silk.

C. Pass the proximal end of the pulmonary artery catheter (Swan Ganz) to an assistant for connection to a continuous flush transducer system.

D. Flush the distal and proximal ports with heparin solution, remove all bubbles, and check balloon integrity by inflating 2 cc of air. Check pressure transducer by quickly moving the distal tip and watching monitor for response.

E. Pass the catheter through the introducer into the vein, then inflate the balloon with 1.0 cc of air, and advance the catheter until the balloon is in or near the right atrium.

F. The approximate distance to the entrance of the right atrium is determined from the site of insertion:

Right internal jugular vein: 10-15 cm.
Subclavian vein: 10 cm.
Femoral vein: 35-45 cm.

G. Advance the inflated balloon, while monitoring pressures and wave forms as the PA catheter is advanced. Watch for ventricular ectopy during insertion. Advance the catheter through the right ventricle into the main pulmonary artery until the catheter enters a distal branch of the pulmonary artery and is stopped by impaction (as evidenced by a pulmonary wedge pressure wave form).

H. Do not advance catheter with balloon while deflated, and do not withdraw the catheter with the balloon inflated. After placement, obtain a chest X-ray to ensure that the tip of catheter is no farther than 3-5 cm from the mid-line, and no pneumothorax is present.

14 Pulmonary Artery Catheter Values

Normal Pulmonary Artery Catheter Values

Right atrial pressure	1-7 mm Hg
RVP systolic	15-25 mm Hg
RVP diastolic	8-15 mm Hg
Pulmonary artery pressure	
PAP systolic	15-25 mm Hg
PAP diastolic	8-15 mm Hg
PAP mean	10-20 mm Hg
PCWP	6-12 mm Hg
Cardiac output	3.5-5.5 L/min
Cardiac index	2.0-3.2 L/min/m^2
Systemic Vascular Resistance	800-1200 dyne/sec/cm^2

Cardiology

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Myocardial Infarction

I. Diagnosis of Acute Myocardial Infarction

- **A.** MI may be associated with a constricting or squeezing sensation in the chest rather than pain per se; pain can radiate to the upper abdomen, back, either arm, either shoulder, neck, or jaw. Pain is of greater severity or longer duration (usually at least 30 minutes) than is seen with unstable angina.
- **B.** Assess the presence of cardiac risk factors and personal or family history of myocardial infarction.
- **C.** Diabetic patients may report unusual symptoms, such as a fluttering sensation, nausea, dyspnea, severe fatigue, or generalized malaise. Silent MI is more common among diabetics.
- **D.** Women tend to have more GI symptoms during acute MI than men.
- **E.** In younger patients without risk factors, cocaine-induced MI should be considered. Cocaine overdose is associated with pronounced anxiety, tachycardia, hyperpyrexia; consider a toxicology screen.
- **F.** Evaluate patient rapidly with a history, physical exam, and electrocardiogram. Cardiac exam may reveal a S3 or S4; an S4 may be more audible with the patient in the left lateral position

II. Differential Diagnosis of Chest Pain

- **A. Acute Pericarditis.** Characterized by pleuritic-type chest pain and diffuse ST segment elevation.
- **B. Aortic Dissection.** "Tearing" chest pain with uncontrolled hypertension, widened mediastinum and increased aortic prominence on chest x-ray.
- **C. Esophageal Rupture** usually occurs after vomiting; x-ray may reveal air in mediastinum or a left side hydrothorax.
- **D. Acute Cholecystitis** is characterized by right subcostal abdominal pain with anorexia, nausea, vomiting, and fever.
- **E. Acute Peptic Ulcer Disease.** Epigastric pain with melena or hematemesis and anemia.

III. Electrocardiographic Findings in Acute Myocardial Infarction

- **A.** ST segment elevations in two contiguous leads with ST depressions in reciprocal leads are strong predictors of MI and the need for primary angioplasty or thrombolysis. The earliest signs of transmural injury are hyperacute T waves. Q waves occur later.
- **B.** If the ECG is uninterpretable (left bundle-branch block), and the clinical signs strongly indicate an evolving infarct, reperfusion with angioplasty or thrombolytics should still be considered.
- **C.** When the 12-lead ECG suggests an inferior MI, ECG data is obtained from the right precordial leads. ST elevation in leads V_{3R}-V_{5R} (especially V_{4R}) points to right ventricular infarct.
- **D.** About 2% of MI's occur without any ECG abnormalities. A negative result on the ECG does not exclude MI.

IV. Diagnostic Testing

A. Blood for cardiac enzyme studies should be drawn after the ECG, and again every 6-12 hours; obtaining three samples is usually sufficient. CPK with isoenzymes, troponin I or troponin T, myoglobin, and LDH should be measured. CPK levels are often normal early after acute myocardial infarction.

B. Troponin T and Troponin I are cardiac specific markers for acute MI. Myoglobin is found in cardiac and skeletal muscle.

Acute Myocardial Infarction Markers

Marker	Increase	Peak	Return to Normal
CK-MB	3-6 hrs	12-24 hrs	24-72 hrs
Troponin T	2-4 hrs	10-24 hrs	5-14 days
Troponin I	2-4 hrs	10-24 hrs	5-10 days
Myoglobin	2-4 hrs	9-12 hrs	24-36 hrs

C. Echocardiography is useful when theECG is indeterminate in patients with chest pain. Normal left ventricular wall motion confirms the absence of significant transmural ischemia.

1. A localized area of hypokinesia indicates possible coronary thrombosis.

2. Echocardiogram may also reveal aortic dissection, mitral valve prolapse, or pericardial fluid.

V. Emergent Therapy of Myocardial Infarction

A. Primary Angioplasty. Primary PTCA is the most efficient way to restore blood flow and conserve heart muscle when available. Primary PTCA is superior to thrombolysis in patients with anterior wall MI, resulting in a higher survival rate, lower rates of stroke, reinfarction and recurrent ischemia.

B. Thrombolytic Therapy. Time is a critical variable in MI management, and thrombolytics should usually be used if a catheter lab is unavailable and no contraindication exists. Thrombolytics are no longer contraindicated by age older than 75. They may be used up to 24 hours after MI. After 24 hours, the risk of myocardial rupture increases.

C. Indications for Thrombolytic Therapy in Myocardial Infarction

1. Chest pain typical of acute myocardial infarction.

2. Electrocardiography. Changes consistent with acute myocardial infarction (ST-segment elevation $\geq$1 mV in two contiguous leads) or presence of left bundle-branch block pattern.

3. Patients $\leq$75 years may use streptokinase or tPA, if >75 years use streptokinase only. Incidence of hemorrhagic stroke is higher with tPA than streptokinase in patients >75 years old.

D. Relative Contraindications. Absence of ST-segment elevation, cerebrovascular disease, relatively recent surgery (>2 wk), cardiopulmonary resuscitation.

E. Absolute Contraindications. Active internal bleeding, history of

hemorrhagic stroke, head trauma, pregnancy, surgery within 2 weeks, recent non-compressible vascular puncture, uncontrolled hypertension (systolic BP >180 and/or diastolic >110 mmHg.

F. Streptokinase (Streptase) is the most commonly used and least expensive thrombolytic; it offers about the same benefit as tPA for patients older than 75 and for those with inferior infarctions; streptokinase confers greater benefit for patients presenting 6 hours or longer after pain onset. Can cause hypotension.

1. IV infusion: 1.5 million IU in 100 mL NS IV over 60 min. Administer methylprednisolone (Solu-Medrol) 250 mg IVP and diphenhydramine (Benadryl) 50 mg IVP prior to streptokinase.
2. Adding IV heparin to streptokinase does not further reduce mortality.

G. Alteplase (tissue plasminogen activator, tPA, Activase)

1. tPA is the quickest-acting thrombolytics; the 90 min patency rate is greater with tPA than SK, but there is no difference at 24 hours.
2. tPA is used for patients who present early (within 4 hours) or who have an anterior MI. Patients who present later, who have a small predicted infarct size, or who are elderly (>75 yrs) and at increased risk for stroke, should be given streptokinase. tPA is considered if there was a known streptococcal infection within 6 months.
3. **Front-loaded Regimen:** IV bolus of 15 mg, then 0.75 mg/kg (up to 50 mg) over 30 min, followed by 0.5 mg/kg (up to 35 mg) infused over next 60 min, with max dose of 100 mg delivered over 1½ hours. Initiate IV heparin concurrently.
4. Intravenous heparin is used to prevent infarct artery reocclusion with tPA. Heparin 5000 U IVP is given prior to tPA, followed by 1000 U/hr, beginning at the end of tPA infusion.

H. Anistreplase (Anisoylated Plasminogen Streptokinase Activator Complex, APSAC, Eminase):

1. Anistreplase is the agent of choice when ease of administration is important, as in prehospital therapy, because it is given as a single IV injection rather than a slow IV drip.
2. One IV bolus of 30 U, given over 2-5 min. Pretreat with methylprednisolone 250 mg IVP and diphenhydramine 50 mg IVP.

VI. Drug Therapy for Acute Myocardial Infarction

A. Aspirin

1. Patients with any sign of an acute coronary syndrome should immediately chew and swallow 160-325 mg of aspirin. Follow with 80-325 mg enteric coated aspirin PO daily.
2. Aspirin is appropriate for either MI or unstable angina. In MI this drug decreases risk for the mortality by 25%.

B. Beta Blockers

1. Patients with reflex tachycardia, systolic hypertension, continuing ischemic pain, or atrial fibrillation with fast ventricular response are excellent candidates for beta-blocker therapy.
2. **Contraindications to beta blockers:** Systolic pressure <100 mm Hg, pulse rate <50 beats per minute, second- or third-degree heart block, severe heart failure, active bronchospastic lung disease.
3. **Atenolol (Tenormin)**, 5 mg IV given over 5 minutes and repeated in 10 minutes if the pulse rate is more than 60 beats per minute; 100 mg PO qd
4. **Metoprolol (Lopressor)**, 5 mg IV push every 5 minutes for three

doses if tolerated; followed by oral maintenance therapy, 100 mg bid.

5. **Propranolol (Inderal)** 40-80 mg PO q6-8h (160-240 mg/d) or Inderal-LA, 80-120 mg PO qd [60, 80, 120, 160 mg].

C. Angiotensin Converting Inhibitors

1. ACE-inhibitors improve survival and decrease morbidity in patients with asymptomatic left ventricular dysfunction after myocardial infarction. ACE-inhibitor use for myocardial infarction patients is highly recommended for all patients.
2. An ACE-inhibitor should be started within 24 hours of acute MI.
3. Captopril (Capoten), initial dose 6.25-12.5 mg PO, titrate to a target dose of 25 mg po tid; maximum of 50 mg PO tid as tolerated.

D. Nitroglycerin

1. Intravenous nitroglycerin should be given to patients with unstable angina and suspected MI as early as possible, unless hypotension is present.
2. Start infusion at a rate of 5-10 mcg/min and titrate to chest pain. Continue for 48 hours; then, if free of chest pain, wean by gradually decreasing the rate of infusion. Oral or topical nitrates are substituted after stabilization.

E. Heparin

1. Initial 5000 units (75 U/kg) bolus, and an infusion of 1000 U/hr (15 U/kg).
2. Adjust heparin to prolong the partial thromboplastin time (PTT) to 2-2.5 times control. Continue heparin for 48-72 hours.
3. In patients not receiving intravenous heparin, prophylactic heparin is recommended (5,000 U SQ bid) to prevent venous thrombosis (or 12,500 U SQ bid in patients with anterior MI who are at risk for mural thrombus formation).
4. Warfarin following MI has a very high complication rate.

F. Lidocaine (Xylocaine)

1. Lidocaine should not be routinely administered to patients with myocardial infarction.
2. Lidocaine should be administered only to patients who have more than six premature ventricular contractions (PVCs) per minute, closely coupled PVCs (the R-on-T phenomenon), multiform PVCs, nonsustained or sustained ventricular tachycardia or fibrillation.

G. Calcium Channel Blockers are useful for hypertension and stable angina pectoris, but they are not recommended for patients with MI.

H. Magnesium has not been shown to produce a benefit and should not be used routinely for MI.

Congestive Heart Failure

I. Clinical Evaluation of Heart Failure

A. All patients who complain of paroxysmal nocturnal dyspnea, orthopnea, or new-onset dyspnea on exertion should undergo evaluation for heart failure.

B. Chest pain may indicate that ischemia is the cause of heart failure; however, ischemia can also occur without chest pain, and can still cause depression of ventricular function.

C. Ascertain any history of edema, heart murmur, prior viral illness, hypertension, myocardial infarction, alcohol or drug use, thyroid disease, anemia, lung disease. Determine the degree of physical impairment.

II. Physical Exam Findings

A. Elevated jugular venous pressure and a third heart sound are the most specific findings, and they are virtually diagnostic in patients with compatible symptoms.

B. Pulmonary rales or peripheral edema are relatively nonspecific findings.

C. Patients with symptoms highly suggestive of heart failure should undergo echocardiography or radionuclide ventriculography to determine left ventricular ejection fraction, and valvular status.

D. Abdominal jugular reflex is a better clinical indicator of heart failure than pulmonary rales. Press on the patient's abdomen and observe jugular veins for distension.

Conditions That Mimic or Provoke Heart Failure

Coronary artery disease and myocardial infarction	Tachyarrhythmias or bradyarrhythmias
Hypertension	Pulmonary embolism
Aortic or mitral valve disease	Pulmonary disease
Cardiomyopathies: Hypertrophic, idiopathic dilated, postpartum, genetic, toxic, nutritional, metabolic	Congenital abnormalities
	High output states: Anemia, hyperthyroidism
Myocarditis: Infectious, toxic, immune	A-V fistulas, Paget's disease, fibrous dysplasia, multiple myeloma
Pericardial constriction	Renal failure, nephrotic syndrome

III. Laboratory Evaluation of Heart Failure

A. CXR, EKG, echocardiogram.

B. Electrolytes, BUN, creatinine, albumin, liver function tests, Mg

C. CBC, urinalysis

D. Thyroxine and thyroid stimulating hormone (if atrial fibrillation, evidence of thyroid disease, or age >65 yrs)**Chest Roentgenogram.** Cardiomegaly, pleural effusions, pulmonary vascular redistribution, Kerley's lines, perivascular cuffing, alveolar edema, and/or infiltrate may be seen.

E. Electrocardiogram. Often evidence of old myocardial infarction, hypertrophy, and/or conduction system delays.

F. Echocardiography or Radiographic Ventriculography

1. Left ventricular function evaluation by measurement of left ventricular performance is a critical step in the evaluation and

management of patients with suspected or apparent heart failure.

2. Echocardiography or radiography ventriculography are used to differentiate between dilated cardiomyopathy, left ventricular diastolic dysfunction, valvular heart disease, or a noncardiac etiology.
3. **Left Ventricular Ejection Fraction.** Most patients with heart failure are found to have ejection fractions of less than 40%.

Clinical Evaluation of Laboratory Studies

Test	Finding	Possible Diagnosis
Electrocardiogram	Acute ST-T wave changes Atrial fibrillation, other tachyarrhythmia Bradyarrhythmias Previous myocardial infarction (Q waves) Low voltage Left ventricular hypertrophy	Myocardial ischemia Thyroid disease or heart failure caused by rapid ventricular rate Heart failure due to low heart rate Heart failure due to reduced left ventricular performance Pericardial effusion Diastolic dysfunction
Complete blood count	Anemia	Heart failure related to decreased oxygen-carrying capacity
Urinalysis	Proteinuria	Nephrotic syndrome
BUN/CR ratio	Elevated	Prerenal azotemia
Free T4, thyroid-stimulating hormone	Abnormal	Heart failure because of hypothyroidism or hyperthyroidism

IV. Management of Congestive Heart Failure

A. Indications for Hospitalization

1. Clinical or electrocardiographic evidence of acute myocardial ischemia
2. Pulmonary edema or severe respiratory distress
3. Oxygen saturation below 90 percent
4. Severe complicating medical illness
5. Anasarca
6. Symptomatic hypotension or syncope
7. Heart failure refractory to outpatient therapy

B. Angiotensin Converting Enzyme Inhibitors

1. ACE inhibitors should be prescribed for all patients with left ventricular systolic dysfunction unless contraindicated (potassium >5.5 mMol/L, symptomatic hypotension, renal artery stenosis).
2. Diuretics should be added if symptoms persist despite treatment with ACE inhibitors.
3. ACE-inhibitors have an enhanced first-dose response that may occur in patients with hyponatremia or dehydration; very low initial doses should be prescribed.

C. Diuretics

1. Diuretics are useful for reducing symptoms of volume overload, including orthopnea and paroxysmal nocturnal dyspnea. Diuretics should be started immediately when patients present with symptoms or signs of volume overload.
2. Diuretics reduce intravascular volume and reduce preload.
3. Adequate diuretic dosage is indicated by neck veins that are flat and by the absence of peripheral edema.
4. Loop diuretics (furosemide [Lasix], torsemide [Demadex]) are diuretics of first choice. Severe congestive symptoms require a twice daily regimen because of fluid accumulation during the day. The second daily dose should be given by mid-afternoon to avoid nocturnal diuresis.
5. **Adverse Effects** Orthostatic hypotension, hypokalemia, hypomagnesemia (predisposing to arrhythmias), and hyperuricemia may occur.
6. Serum magnesium and potassium levels should be monitored and supplemented when necessary.

D. Digoxin

1. Digoxin increases the force of ventricular contraction in patients with left ventricular systolic dysfunction. Digoxin improves physical functioning and symptoms, and the hospital readmission rate is reduced; however, mortality is not affected.
2. Digoxin should be initiated along with ACE inhibitors and diuretics in patients with severe heart failure.
3. Patients with mild to moderate heart failure will often become asymptomatic with optimal doses of ACE inhibitors and diuretics, and these patients do not require digoxin. Digoxin should be added to the regimen if symptoms persist despite optimal doses of ACE inhibitors and diuretics.
4. Digoxin level should be kept between 1.0 and 2.0 ng.

Drugs Used in the Management of Heart Failure

Drug	Initial Dose	Target Dose	Max Dose	Adverse Reactions
Loop Diuretics Furosemide (Lasix)	10-40 mg qd	As needed	240 mg bid	Hypomagnesemia, hypokalemia, hyperglycemia, hyperuricemia.
Torsemide (Demadex)	5-10 mg qd	20-40 mg qd	100 mg bid	Hypokalemia, hypomagnesemia, hyperuricemia.
Bumetanide (Bumex)	0.5 mg qd	1-2 mg qd	2 mg bid	Hypokalemia, hypomagnesemia, hyperuricemia.

ACE-Inhibitors Enalapril (Vasotec)	2.5 mg bid	10 mg bid	20 mg bid	Hypotension, hyperkalemia, renal insufficiency, cough, skin rash, angioedema, neutropenia
Lisinopril (Prinivil, Zestril)	2.5-5 mg qd	10-20 mg qd	40 mg qd	Same as enalapril
Quinapril (Accupril)	5 mg bid	10 mg bid	20 mg bid	Same as enalapril
Captopril (Capoten)	6.25-12.5 mg tid	25 mg tid	50 mg tid	Same as enalapril
Digoxin	0.125-0.25 mg qd	As needed	As needed	Atrioventricular block, visual changes, nausea, dizziness, ventricular tachycardia or fibrillation

E. Anticoagulation. Routine anticoagulation for heart failure is not recommended. Patients with an ejection fraction of <25%, a history of systemic pulmonary embolism, or atrial fibrillation may receive warfarin to an INR of 2.0-3.0.

F. Beta Blockers

1. Low-dose beta blockers may produce long-term improvements in heart failure. In patients with catecholamine excess, beta blockers may be very beneficial. However, beta blockers may also cause acute deterioration.
2. **Carvedilol (Coreg)**
   - **a.** Non-selective beta and alpha-1 blocker with significant afterload reducing properties. It improves cardiac index and survival.
   - **b.** It should be considered in all heart failure patients if they are limited by symptoms or are deteriorating on conventional therapy. Initiate at low dosage and increase dose slowly; 6.25-50 mg bid.
3. **Metoprolol (Lopressor)** may be given to patients with compensated CHF at 6.25 mg PO bid for 1 week followed by a doubling of the dose every week as tolerated until 50 mg bid or symptoms appear.

V. Inotropic Agents for Cardiogenic Shock

A. Dobutamine 2.5-10 µg/kg/min, max of 14 µg/kg/min (500 mg in 250 mL D5W, 2 µg/mL) titrate to CO >4, CI >2.

B. Milrinone (Primacor) 50 mcg/kg IV over 10 min, followed by 0.375-0.75 (average 0.5) mcg/kg/min IV infusion (40 mg in 200 mLs NS (QS), conc=0.2 mg/mL). Milrinone is arrhythmogenic.

C. Vesarinone is an inotropic agent with possible antiarrhythmic properties. Its use is associated with reduced mortality; 60 mg PO qd

VI. Revascularization

A. Coronary artery disease is the most common cause of heart failure, and some patients may benefit from revascularization. In particular, patients

with viable myocardium, subserved by substantially stenotic vessels, may obtain benefits if stenosis is relieved.

B. In patients without a history of myocardial infarction or significant angina, physiologic tests for ischemia (thallium scanning) or coronary angiography should be completed.

C. Patients with heart failure who have exercise-limiting angina, angina at rest, or recurrent acute pulmonary edema should undergo coronary artery angiography.

VII. Non-Pharmacologic Measures

A. Patients should be informed about symptoms of worsening heart failure, and they should keep a record of their daily weights. If worsening of symptoms or a weight gain of 3-5 lb or more occurs within one week, the patient should inform the physician and take an extra dose of diuretic.

B. Activity. Regular exercise is encouraged.

C. Diet

1. Dietary sodium should be restricted to 2 g per day.

2. Total fluid intake of 1.5-2 L/day should be maintained, and excessive fluid intake should be avoided. Fluid restriction is not advisable unless hyponatremia is present.

3. Alcohol should be discouraged, and patients should consume no more than one drink per day.

Atrial Fibrillation

I. Clinical Evaluation

A. Atrial fibrillation (AF) may manifest only as fatigue because of impaired cardiac output; palpitations, shortness of breath or chest pain may also occur. Vague symptoms, such as lack of energy or a change in sense of well-being, or no symptoms may be noted. Syncope may infrequently accompany AF. Symptoms of myocardial ischemia and angina may be caused by the rapid ventricular rate.

B. Paroxysmal AF may cause symptoms that abate and recur, especially with physical exertion or emotional stress.

C. The cause of the atrial fibrillation should be identified once the ventricular rate has been controlled.

D. Precipitating causes such as hyperthyroidism, electrolyte abnormalities, and drug toxicity (theophylline) should be excluded. Stimulant abuse, excess tobacco, alcohol, caffeine, chocolate, over-the-counter cold remedies, and street drugs should be ruled out.

E. AF may be associated with a recent acute illness, such as pneumonia, or a history of ischemic heart disease.

II. Physical Examination

A. The pulse has an irregular timing and amplitude. Rapid ventricular rate may cause hypotension, pulmonary congestion.

B. Examine the patient for evidence of hypertension, rheumatic fever, valvular disease, pericarditis, coronary artery disease, hyperthyroidism, or chronic obstructive pulmonary disease.

C. The cardiovascular system is evaluated for murmurs or cardiac enlargement on chest x-ray. Peripheral bruits may be a marker for

associated coronary artery disease.

III. Diagnostic Evaluation

A. 12-lead Electrocardiogram reveals irregular R-R intervals with no P waves. Ventricular rate is irregularly irregular. No P-waves will be seen in AF. There is an irregular baseline with rapid fibrillary waves (more than 320 per minute). The usual ventricular response rate is 130-180 per minute.

B. Chest x-ray, electrolytes and screening labs, ECG, echocardiogram, free T4, TSH, and drug levels (theophylline) are assessed.

Causes of Atrial Fibrillation

Hypoglycemia Theophylline intoxication Acute pulmonary disease (pneumonia, asthma, chronic obstructive pulmonary disease, pulmonary embolus) Heavy alcohol intake or alcohol withdrawal Hyperthyroidism Severe acute systemic illness Left or right ventricular failure Mitral valve disease (stenosis or regurgitation) Pericarditis Hypertensive heart disease with left ventricular hypertrophy	Hypertrophic cardiomyopathy Coronary artery defect Atrial septal defect Aortic stenosis Infiltrative diseases (amyloidosis, cardiac tumors) Acute myocardial infarction Lone atrial fibrillation (No underlying disease state) Electrolyte abnormalities Stimulant abuse, excess tobacco, xanthine (tea), chocolate, over-the-counter cold remedies, street drugs.

IV. Emergency Management of Unstable Atrial Fibrillation

A. Patients Who Develop Acute Hypotension, Angina or Heart Failure because of rapid heart rate should be treated as follows:

1. Immediate direct-current cardioversion is administered. Anesthesia or sedation and nasal oxygen are necessary except in an emergency.

2. After cardioversion, rhythm should be stabilized with IV procainamide (Pronestyl), followed by oral maintenance therapy (Procanbid).

3. These patients should also receive a rate control drug (beta-blocker, calcium blocker, or digoxin) for rate control.

V. Initial Management of Stable Atrial Fibrillation

A. Rate Control. Control of the ventricular response is the first goal in patients who do not require immediate cardioversion. Ventricular rate should usually be brought below 100.

B. Beta blockers

1. Beta blockers should receive first consideration for rate control. Digoxin does not promote conversion to normal sinus rhythm, while beta blockers may occasionally have such an effect.

2. Beta blockers have a more rapid onset of action than digoxin. Digoxin may require 6 hours to slow the heart rate. In contrast, the heart rate may decrease within minutes after a beta blocker.

3. Contraindications to Beta-Blockers. Asthma, obstructive lung disease, heart failure.

4. Propranolol (Inderal): IV dose of 1-4 mg at 1 mg/min. A second dose may be given after 2 minutes if necessary. Additional drug should not be given in less than 4 hours. Maintenance: 10-30 mg PO tid-qid.

Drug of choice in patients with atrial fibrillation secondary to hyperthyroidism because it blocks conversion of T3 to T4, in addition to slowing ventricular response rate.

5. **Esmolol (Brevibloc)**: loading dose 0.5 mg/kg IV over 1 minute, followed by a 4 minute infusion of 0.05 mg/kg/min. If an adequate therapeutic effect is not observed within 5 minutes, repeat loading dose, and follow with an infusion increased to 0.1 mg/kg/min. If necessary, repeat loading infusion and increasing maintenance infusion by increments of 0.05 mg/kg/min; max 0.3 mg/kg/min.
6. **Atenolol (Tenormin)** 5-10 mg IV doses; 25-100 mg PO per day.
7. **Metoprolol (Lopressor)** 5 mg IV doses; 25-100 mg PO bid.

C. Calcium Channel Blockers

1. Verapamil or diltiazem are appropriate options if asthma or obstructive lung disease. Diltiazem has less negative inotropic effects than verapamil. Calcium blockers are contraindicated in CHF.
2. Diltiazem (Cardizem): 0.25-mg/kg (15-20 mg) IV bolus over 2 min, followed by an infusion of 5-15 mg/h.
3. Verapamil (Isoptin): IV bolus of 2.5-5 mg over 2 minutes.

D. Digoxin is useful in patients with left ventricular systolic dysfunction.

1. Digoxin may be harmful, in left ventricular diastolic dysfunction (hypertensive heart disease and hypertrophic cardiomyopathy). Beta blockers or calcium blockers are the preferred agents in diastolic dysfunction.
2. **Loading dose:** 0.5 mg IV/PO, then 0.25 mg IV q4h x 2-3 doses followed by 0.125-0.25 mg/day IV/PO. Decrease dose in renal failure.

VI. Intermediate Management of Stable Atrial Fibrillation

A. Restoration of Sinus Rhythm

1. After ventricular rate has been controlled, cardioversion should be considered. Restoration of sinus rhythm improves cardiac output and reduces the risk of systemic embolization.
2. Sinus rhythm can be restored by IV loading of an antiarrhythmic drug. If pharmacologic therapy is ineffective, direct-current cardioversion is considered.

B. Factors that Identify Inability to Remain in Sinus Rhythm

1. The most important factors are duration of fibrillation and the degree of left atrial dilation.
2. Mitral valve disease, cardiomyopathy, pulmonary disease, and binge alcohol drinking will also prevent conversion.

C. Anticoagulation

1. Anticoagulation is initiated before cardioversion if atrial fibrillation has been present >48-72 hours (unless transesophageal echocardiography has excluded the presence of thrombus).
2. Patients should receive warfarin (Coumadin) for 3-4 weeks before the procedure; maintain INR of 2.0-3.0.
3. After successful cardioversion, warfarin is continued for 4 weeks, because fully effective atrial contraction is delayed.

VII. Antiarrhythmic Drug Therapy

A. Type IA agents: Quinidine, procainamide, and disopyramide. Patients taking type IA antiarrhythmics should be monitored closely for proarrhythmic complications. Marked prolongation of the QT interval is an indication of impending Torsades de pointes arrhythmia.

1. **Quinidine (Quinaglute).** Conversion success rate is 50-60%. The dosage of quinidine gluconate is 324 mg PO tid-qid. IV or IM quinidine is used only if the oral route is unavailable.
2. **Procainamide (Pronestyl)**
   a. 43-58% convert to sinus rhythm with IV administration of procainamide.
   b. Loading dose is 15 mg/kg at 20 mg/min IV, followed by an infusion of 1-4 mg/min. Procainamide caps 250-500 mg PO q4-6h or procainamide SR (Procanbid) 500-1000 mg PO bid. Long-term use may lead to increased antinuclear antibody and to a lupus erythematosus-like syndrome in 30%.
3. **Disopyramide** is a third-line agent because of potent negative inotropic and anticholinergic properties.

B. Type IC antiarrhythmic drugs, flecainide (Tambocor) and propafenone (Rythmol) have a negative inotropic and proarrhythmic effects.

C. Class III antiarrhythmics

1. **Amiodarone (Cordarone)** has a major advantage over other antiarrhythmic agents because it maintains sinus rhythm more frequently and has fewer proarrhythmic effects than other agents. Loading dose is 400 mg bid-tid PO for 1-3 weeks; gradually reduce to a maintenance dosage of 200 qd after 6-8 weeks. The IV dose is 150 mg over 10 min, then 1 mg/min IV infusion x 6 hours, followed by 0.5 mg/min IV infusion. Monitor for pulmonary toxicity, hepatic dysfunction, visual impairment, and thyroid abnormalities. Amiodarone doubles the prothrombin time in patients taking warfarin.
2. **Sotalol (Betapace)** has less toxicity than amiodarone and is well-tolerated; useful if other drugs fail. Initial dosage: 80 mg PO bid, increasing prn to 240-320 mg/d, divided bid-tid. Significant beta-blocking activity and may cause bradycardia and Torsades de pointes arrhythmia.
3. **Ibutilide (Corvert)** is used for conversion. Conversion rates are about 40%. Used for acute conversion only, not for maintenance; 1 mg IV over 10 min; may repeat dose after 10-15 minutes.

VIII. Elective Direct-Current Cardioversion

A. The ventricular rate should be controlled and the patient anticoagulated before elective cardioversion if AF has been present >48-72 hours.

B. Patients undergoing elective DC cardioversion should receive an antiarrhythmic agent before cardioversion.

C. Digoxin level should be checked because digoxin toxicity may predispose to ventricular fibrillation or asystole after cardioversion. Electrolyte imbalances, especially a low potassium, should be corrected.

D. Administer midazolam (Versed) and manage the airway.

E. Conversion usually can be accomplished with 50 to 100 joules (J), but up to 360 J may be required.

IX. Long-Term Management of Chronic Atrial Fibrillation

A. Stroke Prevention Therapy

1. Aspirin and warfarin reduce the risk of stroke in atrial fibrillation. The selection of an antithrombotic agent should be based on the risk for stroke and suitability for anticoagulation.
   a. **Risk Factors for Stroke** include increasing age (>75 years), previous stroke or transient ischemic attack, hypertension, diabetes, heart failure, myocardial ischemia, or valvular disease.

2. **Patients less than 60 years of age with lone atrial fibrillation (no risk factors)** have an extremely low risk for stroke and do not benefit from antithrombotic agents.
3. **Patients 60-75 years of age with no risk factors** are adequately protected with aspirin 325 mg/d.
4. **Patients with one or more risk factors, or who are over 75 years of age**, should receive warfarin, adjusted to an INR of 2.0-3.0.
5. Aspirin is an alternative for high-risk patients with a contraindication to warfarin, including noncompliant patients. Ticlopidine (Ticlid), 250 mg bid, may be used if unable to tolerate aspirin.

Hypertensive Emergencies

I. Clinical Evaluation of Hypertensive Syndromes

A. Severe hypertension is characterized by diastolic blood pressure (BP) higher than 120 mmHg or systolic BP higher than 180 mmHg.

B. Hypertensive Emergency is defined by a diastolic blood pressure >120 mmHg with ongoing vascular damage. Symptoms or signs of neurologic, cardiac, renal, or retinal dysfunction are present.

1. Hypertensive emergencies include severe hypertension in the following settings:

a. Aortic dissection
b. Acute left ventricular failure and pulmonary edema
c. Acute renal failure or worsening of chronic renal failure
d. Hypertensive encephalopathy
e. Focal neurologic damage indicating thrombotic or hemorrhagic stroke
f. Pheochromocytoma, cocaine overdose, or other hyperadrenergic states
g. Unstable angina or MI

C. Hypertensive Urgency is defined as diastolic blood pressure >120 mmHg without evidence of vascular damage; the disorder is asymptomatic and no retinal lesions are present.

D. Causes of Secondary Hypertension. Renovascular hypertension, pheochromocytoma, cocaine use, withdrawal from alpha$_2$ stimulants, beta blockers, or alcohol; noncompliance with antihypertensive medications.

II. Initial Assessment of Severe Hypertension

A. When severe hypertension is noted, the measurement should be repeated in both arms to detect any significant differences.

B. Peripheral pulses are assessed for absence or delay. Evidence of pulmonary edema, is sought. The initial assessment should also determine how ill the patient appears.

C. Target organ damage is evidenced by chest pain, neurologic signs, altered mental status, profound headache, dyspnea, abdominal pain, hematuria, focal neurologic signs (paralysis or paresthesia), and hypertensive retinopathy.

D. Prescription drug use should be assessed, including the possibility of a missed dose of antihypertensive therapy. Ask about recent cocaine or amphetamine use.

E. If focal neurologic signs are present, a CT scan may be required to differentiate hypertensive encephalopathy from a stroke syndrome. In stroke syndromes, hypertension may be transient and secondary to the neurologic event; the neurologic deficits are fixed and follow a predictable neuroanatomic pattern. By contrast, in hypertensive encephalopathy, the neurologic signs follow no anatomic pattern, and there is diffuse alteration in mental function.

III. Laboratory Evaluation

A. Complete blood cell count, urinalysis for protein, glucose, and blood; urine sediment examination for cells, casts, and bacteria; full chemistry panel (SMA-18).

B. If chest pain is present, cardiac enzymes are obtained.

C. If the history suggests a hyperadrenergic state, exclude the possibility of a pheochromocytoma with a 24 hour urine for metanephrines, plasma catecholamines. A urine drug screen may be necessary to exclude illicit drug use.

D. Electrocardiogram.

E. A workup for secondary hypertension is often necessary to rule out primary aldosteronism (24 hour urine potassium, plasma renin activity), or renal artery stenosis (captopril renography, intravenous pyelography).

Screening Tests for Secondary Hypertension

Renovascular Hypertension	Captopril Test Captopril Renography Intravenous Pyelography MRI Angiography Arteriography (DSA)
Hyperaldosteronism	Serum Potassium 24 hr Urine Potassium Plasma Renin Activity CT Scan of Adrenals
Pheochromocytoma	24 hr urine Metanephrine Plasma Catecholamine level CT Scan Nuclear MIBG Scan
Cushing's Syndrome	Plasma ACTH Dexamethasone Suppression Test
Hyperparathyroidism	Serum Calcium Serum Parathyroid hormone

IV. Management of Hypertensive Emergencies

A. The patient is hospitalized for bed rest, intravenous access, continuous intra-arterial blood pressure monitoring, and electrocardiographic monitoring. Volume status and urinary output are monitored.

B. A rapid, uncontrolled reduction in blood pressure may cause coma, stroke, myocardial infarction, acute renal failure, or death.

C. **Controlled BP Reduction** should reduce BP by approximately 20% of its initial value in the first hour with an IV agent, followed by more

gradual over the next 12-24 hours. Maintenance oral antihypertensive therapy should be initiated as soon as possible.

V. Parenteral Antihypertensive Agents

A. Nitroprusside (Nipride)

1. Drug of choice in almost all hypertensive emergencies (except myocardial ischemia or renal impairment). Dilates both arteries and veins, and reduces afterload and preload.
2. Onset is nearly instantaneous, and effects disappear approximately 1-10 minutes after discontinuation.
3. The starting dosage is 0.25-1.0 mcg/kg/min by continuous infusion with a range of 0.25-8 mcg/kg/min. Titrate to gradually reduce pressure.
4. When treatment is prolonged or when renal insufficiency is present, the risk of cyanide toxicity is increased. Signs of thiocyanate toxicity include anorexia, disorientation, fatigue, hallucinations, nausea, toxic psychosis and seizures. Clinical deterioration with cyanosis, metabolic acidosis, and arrhythmias indicates cyanide toxicity.

B. Nitroglycerine

1. Drug of choice for hypertensive emergencies with coronary ischemia. Should not be used with hypertensive encephalopathy because it increases intracranial pressure.
2. The starting dose is 15 mcg IV bolus, then 5-10 mcg/min (50 mg in 250 mL D5W). Titrate by increasing dose at 3-5-minute intervals up to 100-200 mcg/min (2-3 mcg/kg/min).
3. Nitroglycerine decreases venous capacitance, venous return, left ventricular filling pressure, and cardiac output.
4. Rapid onset of action of 2-5 minutes. Tolerance may occur within 24-48 hours.

C. Labetalol IV (Normodyne)

1. Good choice if BP elevation is associated with hyperadrenergic activity. Drug of choice for aortic thoracic or aortic abdominal aneurysm.
2. The alpha-blockade of labetalol reduces peripheral vascular resistance while the beta-blocking action prevents reflex tachycardia. Use 20 mg of labetalol slow IV over 2 mins; monitor BP q5min. Additional doses of 20-80 mg may be administered q5-10min, then q3-4h prn or 2 mg/min IV infusion.
3. The onset of action is approximately 5 minutes, and maximum effect occurs 30 minutes after each dose. Effects persist for 3-6 hours.

D. Nicardipine IV (Cardene IV)

1. A fast-acting calcium channel blocker that shares many of the predictable antihypertensive qualities of nitroprusside.
2. Nicardipine infusion is started at 5 mg/h and may be increased to 15 mg/h; BP is usually controlled at 7.5 mg/h. Its onset of action is 5-10 minutes, and its effects cease 10-15 minutes after discontinuation.

E. Phentolamine is used in pheochromocytoma; 2-5 mg boluses every 5-10 minutes. Nitroprusside is more titratable, and is a better choice.

F. Trimethaphan. Used for dissecting aortic aneurysms. Most physicians are unfamiliar with trimethaphan; therefore, nitroprusside is a better choice. Trimethaphan is used only after an intravenous beta blocker has been given.

Ventricular Arrhythmias

I. Ventricular Fibrillation and Tachycardia

-**If unstable (see ACLS protocol page 5)**, defibrillate with unsynchronized 200 J, 300 J, then 360 J.
-Oxygen 100% by mask.
-Lidocaine loading dose 50-100 mg IV, then 2-4 mg/min IV **OR**
-Procainamide loading dose 10-15 mg/kg at 20 mg/min IV or 100 mg IV q5min, then 1-6 mg/min IV maintenance **OR**
-Bretylium loading dose 5-10 mg/kg over 5-10 min, then 2-4 mg/min IV (may repeat loading dose up to total 30 mg/kg.
-**Also see "other antiarrhythmics" below**.

II. Torsades de pointes

-Correct underlying cause and consider discontinuing drugs that cause Torsades de pointes (quinidine, procainamide, disopyramide, moricizine, sotalol, ibutilide, bepridil, lidocaine, amiodarone, phenothiazines, tricyclic and tetracyclic antidepressants, terfenadine, vasopressin, imidazoles, pentamidine); correct hypokalemia and hypomagnesemia.
-Magnesium sulfate (drug of choice) 1-4 gm in IV bolus over 5-15 min or infuse 3-20 mg/min for 7-48h until QT interval <0.5 sec.
-Isoproterenol (Isuprel) 2-20 µg/min (2 mg in 500 mL D5W, 4 µg/mL) **OR**
-Phenytoin (Dilantin) 100-300 mg IV given in 50 mg aliquots q5min.
-Consider ventricular pacing and cardioversion.

III. Other Antiarrhythmics

Class Ib

-Lidocaine 50-100 mg IV, then 2-4 mg/min IV.
-Mexiletine (Mexitil) 100-200 mg PO q8h, max 1200 mg/d.
-Tocainide (Tonocard) loading 400-600 mg PO, then 400-600 mg PO q8-12h; max 1800 mg/d.
-Phenytoin (Dilantin), loading dose 100-300 mg IV given as 50 mg in NS over 10 min IV q5min, then 100 mg IV q5min prn.

Class Ic

-Flecainide (Tambocor) 50-100 mg PO q12h, max 400 mg/d.
-Propafenone (Rythmol) 150-300 mg PO q8h, max 1200 mg/d.

Class III

-Amiodarone (Cordarone) PO loading 400-1200 mg/d in divided doses x 5-14 days, then 200-400 mg PO qd (5-10 mg/kg) **OR**
150 mg slow IV over 10 min, then 1 mg/min IV infusion x 6 hours then 0.5 mg/min IV infusion thereafter.
-Sotalol (Betapace) 40-80 mg PO bid, max 320 mg/d in 2 divided doses.
-Bretylium 5-10 mg/kg IV over 5-10 min, then maintenance of 1-4 mg/min IV or repeat boluses 5-10 mg/kg IV q6-8h; infusion of 1-4 mg/min IV.

Labs: SMA 12, Mg, calcium, CBC, cardiac enzymes, LFT's, ABG, drug levels, thyroid function test. ECG, electrophysiologic study.

Pericarditis

Labs: CBC, SMA 12, albumin, Viral serologies: Coxsackie A & B, measles, mumps, influenza, ASO titer, hepatitis surface antigen, ANA, rheumatoid factor, anti-myocardial antibody, PPD with candida, mumps. Cardiac enzymes q8h x 4, ESR, complement thyroid panel, PT/PTT, blood C&S X 2. ECG, echocardiogram, CXR PA & LAT.

Pericardiocentesis: Gram stain, C&S, Thayer-Martin culture for gonococcus, cell count & differential, cytology, glucose, protein, LDH, amylase, triglyceride, AFB, fungal, specific gravity, pH, LE prep, rheumatoid factor.

Nonpurulent Pericarditis

-Aspirin 650 mg PO q4-6h (2-3 gm/d) **OR**
-Indomethacin (Indocin) 25-75 mg PO tid **OR**
-Ibuprofen 400 mg PO tid or qid
-Morphine 2-4 mg IV q10 min prn pain; narcotics should be used cautiously if possible tamponade or constriction-may cause hypotension **OR**
-Meperidine 50-100 mg IV q4h prn pain and Promethazine (Phenergan) 25-75 mg IV q4h.
-Prednisone 40-60 mg PO qd.

Purulent Pericarditis

-Nafcillin or Oxacillin 2 gm IV q4h **AND EITHER**
-Gentamicin or tobramycin 100-120 mg IV (1.5-2 mg/kg); then 80 mg (1.0-1.5 mg/kg) IV q8h (adjust in renal failure) **OR**
-Ceftizoxime 1-2 gm IV q8h.
-Vancomycin, 1 gm IV q12h, may be used in place of nafcillin or oxacillin.

Temporary Pacemakers

Temporary Pacemakers: Placed acutely for life threatening conduction blocks and bradycardia.

Transvenous Pacemakers: Inserted into the right heart via the subclavian, femoral vein, or jugular veins. The generator is attached to the leads.

External Pacemakers: Place one paddle posteriorly between the scapulae, and the other on the sternum. An external pace maker is a temporary measure until a transvenous pacer can be inserted.

Indications:

Prophylactic: New right bundle branch block (RBBB) with left heart block (LHB), alternating bundle branch block (BBB), Mobitz type II, complete heart block.

Therapeutic: Symptomatic bradycardia unresponsive to medical therapy; heart rate <50 with symptoms; sequential pacing of atria and ventricles when hemodynamically compromised by AV dissociation.

Management of Transvenous Pacer Problems:

-If the patient is unstable, place the external pacer paddles on and tum output up until capture occurs.
-If the pacer does not capture, turn the output to maximum voltage. If this measure fails, try turning the sensitivity up (lower threshold voltage). Change batteries or change units.
-Order daily potable CXR to rule out pneumothorax and check lead placement.

-Record daily threshold measurements

Permanent Pacemakers

General Considerations: Leads are placed transvenously either in the right ventricle, right atrium, or both. Leads are attached to a pulse generator that is sutured below the skin.

Five Position Pacemaker Code

Chamber Paced	Chamber Sensed	Response to Sensing	Programmable functions	Anti-tachycardia functions
Ventricle	Ventricle	Triggers	Programmable	Programm-able
Atrium	Atrium	Inhibits	Multiprogrammable	Shock
Double	Double	Double: T or I	Communicates	Double: P and S
O-none	O-none	O-none	Rate modulation	

Most pacemakers are VVI or DDD.

Indications for Permanent Pacemakers:

Complete heart block (regardless of symptoms).

Mobitz II if symptomatic

BBB with or without symptoms (depending on patterns)

Sick Sinus Syndrome if symptomatic or if beta blocker or calcium blocker therapy is planned

Carotid sinus hypersensitivity if symptomatic.

Post pacemaker implantation:

Immediate and daily CXR should be ordered to rule out pneumothorax and evaluate lead position. Check wound condition daily.

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Pulmonology

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Airway Management and Intubation

Orotracheal Intubation:

ETT Size (interior diameter):
Women 7.0-9.0 mm
Men 8.0 -10.0 mm.

1. **Prepare functioning suction** apparatus. Have bag and mask apparatus set-up with 100% oxygen; and ensure that patient can be adequately bagged and suction apparatus is available.
2. **If sedation and/or paralysis is required,** consider rapid sequence induction as follows:
   -Fentanyl (Sublimaze) 50 mcg increments IV (1 mcg/kg) **with:**
   -Midazolam hydrochloride (Versed) 1 mg IV q2-3 min, max 0.1-0.15 mg/kg **followed by:**
   -Succinylcholine (Anectine) 0.6-1.0 mg/kg, at appropriate intervals.

   Note: These drugs may cause vomiting; therefore, cricoid cartilage pressure should be applied during intubation (Sellick maneuver).
3. **Position the patient's head** in "sniffing" position with head flexed at neck and extended. If necessary elevate head with a small pillow.
4. **Ventilate patient** with bag mask apparatus and hyperoxygenate with 100% oxygen.
5. **Hold Endoscope handle** with left hand, and use right hand to open patient's mouth. Insert blade along the right side of mouth to the base of tongue, and push the tongue to the left. If using curved blade, advance to the vallecula (superior to epiglottis), and lift anteriorly, being careful not to exert pressure on the teeth. If using a straight blade, place beneath the epiglottis and lift anteriorly.
6. **Place endotracheal tube (ETT)** into right corner of mouth and pass it through the vocal cords; stop just after the cuff disappears behind vocal cords. If unsuccessful after 30 seconds, stop and resume bag and mask ventilation before reattempting. If necessary, use stilette to maintain the shape of the ETT (a hockey stick shape may be helpful); remove stilette after intubation. Application of lubricant jelly at endotracheal tube balloon facilitates passage through the vocal cords.
7. **Inflate cuff with syringe** keeping cuff pressure $\leq$20 cm H_2O and attach the tube to an Ambu bag or ventilator. Confirm bilateral, equal expansion of the chest and equal bilateral breath sounds. Auscultate abdomen to confirm that the ETT is not in the esophagus. If there is any question about proper ETT location, repeat laryngoscopy with tube in place to be sure it is endotracheal; remove tube immediately if there is any doubt about proper location. Secure the tube with tape and note centimeter mark at the mouth. Suction the oropharynx and trachea.
8. **Confirm proper tube placement with a chest X-ray** (tip of ETT should be between the carina and thoracic inlet, or level with the top of the aortic notch).

Nasotracheal Intubation:

Nasotracheal intubation is the preferred method if prolonged intubation is anticipated (increased patient comfort). Intubation will be facilitated if patient is awake and spontaneously breathing. There is an increased incidence of sinusitis with nasotrachael intubation.

1. **Spray nasal passage with a vasoconstrictor** such as cocaine 4% or phenylephrine 0.25% (Neo-Synephrine) may be used. If sedation is required before nasotracheal intubation, administer fentanyl (Sublimaze) 1 mcg/kg with midazolam hydrochloride (Versed) 0.05-0.1 mg/kg.

Lubricate nasal airway with lidocaine ointment.

Tube Size:

Women 7.0 mm tube

Men 8.0, 9.0 mm tube

2. **Place the nasotracheal tube into the nasal passage** and guide it into nasopharynx along a U-shaped path. Monitor breath sounds by listening and feeling the end of tube. As the tube enters the oropharynx, gradually guide the tube downward. If the breath sounds stop, withdraw the tube 1-2 cm until breath sounds are heard again. Reposition the tube, and, if necessary, extend the head and advance. If difficulty is encountered, perform direct laryngoscopy and insert tube under direct visualization, or use Magill forceps.
3. **Successful intubation** occurs when the tube passes through the cords; a cough may occur and breath sounds will reach maximum intensity if the tube is correctly positioned. Confirm correct placement by checking for bilateral breath sounds and expansion of chest.
4. **Confirm proper tube placement** with chest x-ray.

Respiratory Failure and Ventilator Management

I. Indications for Ventilatory Support: Respirations >35, vital capacity <15 mL/kg, negative inspiratory force $\leq$-25, pO2 <60 on 50% O_2, pH <7.2, pCO_2 $>$55, severe, progressive, symptomatic hypercapnia and/or hypoxia, severe metabolic acidosis.

II. Initiation of Ventilator Support

A. Intubation

1. Prepare suction apparatus, laryngoscope, endotracheal tube ($\geq$ No. 8 if possible); clear airway and place oral airway, hyperventilate with bag and mask attached to high flow oxygen.
2. Midazolam (Versed) 1-2 mg IV boluses until sedated.
3. Intubate, inflate cuff, ventilate with bag, auscultate chest, and suction trachea.

B. Initial Orders: FiO_2 = 100%, PEEP = 3-5 cm H_2O, assist control 8-14 breaths/min, tidal volume = 800 mL (10-15 mL/kg ideal body weight), set rate so that minute ventilation (VE) is approximately 10 L/min. Alternatively, use intermittent mandatory ventilation mode with tidal volume and rate to achieve near-total ventilatory support. Consider pressure support in addition to IMV at 5-15 cm H_2O.

C. ABG should be obtained in 30 min, CXR for tube placement, measure cuff pressure q8h (maintain $\leq$20 mm Hg), pulse oximeter, arterial line, and/or monitor end tidal CO_2. Maintain oxygen saturation >90-95%.

D. Ventilator Management

1. **Decreased Minute Ventilation:** Evaluate patient and rule out complications (endotracheal tube malposition, cuff leak, excessive secretions, bronchospasms, pneumothorax, worsening pulmonary disease, sedative drugs, pulmonary infection). Readjust ventilator rate to maintain mechanically assisted minute ventilation of 10 L/min. If peak airway pressure (AWP) is >45 cm H_2O, decrease tidal volume to 7-8 mL/kg (with increase in rate if necessary), or decrease ventilator flow rate.
2. **Arterial Saturation ≥94% and pO_2 >100**, reduce FIO_2 (each 1% decrease in FIO_2 reduces pO_2 by 7 mm Hg); once FIO_2 is <60%, PEEP may be reduced by increments of 2 cm H_2O until PEEP = 3-5 cm H_20. Maintain O_2 saturation of ≥90% (pO_2 >60).
3. **Arterial saturation <90% and pO2 <60,** increase $FI0_2$ up to 60-100%, then consider increasing PEEP by increments of 3-5 cm H_2O (PEEP >10 requires a PA catheter). Add additional PEEP until oxygenation is adequate with an FIO_2 of <60%.
4. **Excessively Low pH,** (pH <7.33 because of respiratory acidosis/hypercapnia): Increase rate and/or tidal volume. Keep peak airway pressure <40-50 cm H_2O if possible.
5. **Excessively High pH** (>7.48 because of respiratory alkalosis/hypocapnia): Reduce rate and/or tidal volume to lessen hyperventilation. If patient is breathing rapidly above ventilator rate, sedate patient.
6. **Patient "Fighting" Ventilator:** Consider IMV or SIMV mode, or add sedation with or without paralysis (exclude complications or other causes of agitation). Paralytic agents should not be used without concurrent amnesia and/or sedation.
7. **Sedation:**
   - **a.** Diazepam (Valium) 2-5 mg slow IV q2h prn agitation **OR**
   - **b.** Lorazepam (Ativan) 1-2 mg IV q1-2h prn sedation **OR**
   - **c.** Midazolam (Versed) 1-2 mg IV boluses until sedated.
   - **d.** Morphine Sulfate 2-5 mg IV q5min, max dose 20-30 mg OR 0.03-0.05 mg/kg/h IV infusion (50-100 mg in 500 mL D5W) titrated **OR**
   - **e.** Propofol (Diprivan): 50 mcg/kg bolus over 5 min, then 5-50 mcg/kg/min.
8. **Paralysis (with simultaneous sedation and/or amnesia):**
   - **a.** Succinylcholine (Anectine) 0.6-1.0 mg/kg; very short acting, T½ 3.5 min **OR**
   - **b.** Vecuronium (Norcuron) 0.1 mg/kg IV, then 0.06 mg/kg/h IV infusion or q1h prn; intermediate acting, T½ 60 min **OR**
   - **c.** Pancuronium (Pavulon) 0.08 mg/kg IV, then 0.03 mg/kg/h infusion or q1h IV prn; long acting, T½ 75 min; may cause tachycardia and/or hypertension **OR**
   - **d.** Atracurium (Tracrium) 0.5 mg/kg IV, then 0.3-0.6 mg/kg/h infusion; short acting, T½ 20 min; because of histamine releasing properties, may cause bronchospasm and/or hypotension.
   - **e.** Monitor level of paralysis with a peripheral nerve stimulator. Adjust neuromuscular blocker dosage to achieve a “train-of-four” (TOF) of 90-95%; if patient on inverse ratio ventilation is used, maintain TOF at 100%.

9. **Loss of Tidal Volume:** If a difference between the tidal volume setting and the delivered volume occurs, check for a leak in the ventilator or inspiratory line. Check for a poor seal between the endotracheal tube cuff or malposition of the cuff in the subglottic area. If a chest tube is present, check for air leak.
10. **Daily weaning parameters** should be obtained when weaning is being considered.

Inverse Ratio Ventilation

1. **Indications:** pAO_2 <60 mm Hg, FIO_2 >0.6, peak airway pressure >45 cm H_2O, or PEEP >15 cm H_2O. Requires heavy sedation and muscle relaxation.
2. **Set oxygen concentration (FIO_2)** at 1.0; inspiratory pressure at ½ to 2/3 the peak airway pressure on standard ventilation; set the inspiration: expiration ratio at 1:1; set rate at ≤15 breaths/min. Maintain tidal volume by adjusting inspiratory pressures. Monitor auto-PEEP level.
3. **Monitor PaO_2**, oxygen saturation (by pulse oximetry), $PaCO_2$, end tidal PCO_2, PEEP, mean airway pressure, heart rate, blood pressure, SVO_2, and cardiac output.
4. **If SaO_2 remains** <0.9, consider increasing I:E ratio (2:1, 3:1), but generally attempt to keep I:E ratio ≤2:1. If SaO_2 remains <0.9, increase PEEP or return to conventional mode. If $PaC0_2$ is excessively high, evaluate tracings to determine appropriate management. If hypotension develops, rule out tension pneumothorax, administer intravascular volume or pressor agents, decrease I:E ratio or return to conventional ventilation mode.

Ventilator Weaning

I. Ventilator Weaning Parameters
- **A.** Patient alert and rested
- **B.** PaO_2 >70 mm Hg on FiO_2 <50%
- **C.** $PaCO_2$ <50 mm Hg; pH >7.25
- **D.** Negative Inspiratory Force (NIF) more negative than -20 cm H_2O
- **E.** Vital Capacity >10-15 mL/kg (800-1000 mL)
- **F.** Minute Ventilation (VE) <10 L/min; respirations <24 breaths per min (at steady state)
- **G.** Maximum voluntary minute ventilation double that of resting minute ventilation
- **H.** PEEP ≤5 cm H_20
- **I.** Tidal volume 5-8 mL/kg
- **J.** Respiratory rate to tidal volume ratio <105
- **K.** No chest wall or cardiovascular instability or excessive secretions.

II. Indications for Termination of Weaning Trial
- **A.** PaO_2 falls below 55 mm Hg
- **B.** Acute hypercapnia
- **C.** Deterioration of vital signs or clinical status (arrhythmia)

III. Rapid T-tube Weaning Method for Short-term (<7 days) Ventilator Patients without Chronic Obstructive Pulmonary Disease

A. Obtain baseline respiratory rate, pulse, blood pressure and arterial blood gases or oximetry. Discontinue sedation, have well rested patient sit in bed or chair. Provide bronchodilators, and suctioning if needed.

B. Attach endotracheal tube to a T-tube with an inspired oxygen concentration 10% greater than previous level; T-tube flow should exceed peak inspiratory flow.

C. After initial 5 minute interval of spontaneous ventilation, resume mechanical ventilation and check oxygen saturation or draw an arterial blood gas sample.

D. If the 5 minute blood gas is acceptable, a 15 minute interval may be attempted. If the 15 minute interval blood gas is adequate, a 30 minute interval may be attempted. After each interval the patient is placed back on the ventilator for an equal amount of time.

E. If the 30 minute interval blood gas is acceptable and the patient is without dyspnea, a 2-hour period may be attempted; and if blood gases are acceptable, extubation may be considered.

IV. T-tube Weaning Method for Prolonged Ventilator Patients or Chronic Obstructive Pulmonary Disease

A. Continue the above weaning trial after the 5 minute and 15 minute intervals; if successful, follow by a 30 minute, 1 hour, 2 hour, 4 hour, 8 hour and 16 hour interval; evaluate oxygen saturation or arterial blood gas after each interval. If the patient deteriorates at any time, return to last successful interval.

B. When patient is able to breathe for 24 hours with acceptable blood gases and without deterioration, extubation may be considered. With T-tube method the weaning trial is not successful unless the PaO_2 remains >55 mmHg without worsening hypercapnia.

V. Intermittent Mandatory Ventilation Weaning Method (IMV)

A. Obtain baseline vital signs, and arterial blood gases or pulse oximetry. Discontinue sedation; consider pressure support of 10-15 cm H_20.

B. Change the ventilator from assist control to intermittent mandatory ventilation mode; or if already on intermittent mandatory ventilation, decrease the rate as follows:

VI. Patients with No Underlying Lung Disease and on Ventilator for a Brief Period (≤1 week)

A. Decrease IMV rate at 30 min intervals by 1-3 breaths per min at each step, starting at a rate of 8 breaths per minute until a rate of zero is reached.

B. If each step is well tolerated and arterial blood gases are adequate (pH >7.30 or 7.35), extubation may be considered when IMV rate is zero.

VII. Patients with Chronic Obstructive Pulmonary Disease or Prolonged Ventilator Support for ≥1 week

A. Begin IMV at frequency 8 breaths/minute, with a tidal volume of 10 mL/kg, with an oxygen concentration 10% greater than previous rate. Monitor end tidal CO_2.

B. Blood gases should be drawn at 30 and 60 minutes after changing to a rate of 8 breaths per minute. If patient tolerates the decreased rate poorly or if arterial blood gases deteriorate, the IMV should be increased until patient's blood gases stabilize.

C. If the patient is able to tolerate a decreased IMV of 8 breaths/minute after 60 minutes, the IMV rate may be decreased to 6 breaths/min with repeat monitoring of oxygen saturation or arterial blood gases after 30 and 60 min.

D. If the patient remains stable, IMV may be decreased to 4 breaths/min followed by 2 breaths per minute; check oxygen saturation or arterial blood gases at 30 and 60 minute intervals.

E. If patient tolerates the IMV rate of zero without deterioration in vital signs or blood gases, a T-tube may be placed. Observe patient for an additional 24 hours before extubation.

F. If deterioration occurs, increase IMV to previously stable rate until the following morning, then reattempt weaning.

VIII. Pressure Support Ventilation

A. Pressure support ventilation is initiated at 5-25 cm H_20. Set level to maintain the spontaneous tidal volume at 7-15 mL/kg.

B. Gradually decrease the level of pressure support ventilation in increments of 3-6 cm H_20 according to the ability of the patient to maintain satisfactory minute ventilation. Extubation can be considered at a pressure support ventilation level of 5 cm H_20.

IX. Problems Associated with Inability to Wean Patient from Ventilator: Bronchospasms, active pulmonary infection, secretions, small endotracheal tube, weakness of respiratory muscle, low cardiac output.

Pulmonary Embolism

Pulmonary embolism is usually caused by an embolism from a thrombosis in the larger veins above the knee. A deep venous thrombosis can be found in at least 80% of cases of pulmonary emboli.

I. Risk Factors For Pulmonary Embolism

A. Venous Stasis: Prolonged immobilization, stroke, myocardial infarction, heart failure, obesity, varicose veins, anesthesia, age > 65 years old.

B. Endothelial Injury: Surgery, trauma, central venous access catheters, pacemaker wires, previous thromboembolic event.

C. Hypercoagulable State: Malignant disease, high estrogen level (oral contraceptives).

D. Hematologic Disorders: Polycythemia, leukocytosis, thrombocytosis, antithrombin III deficiency, protein C deficiency, protein S deficiency, antiphospholipid syndrome, inflammatory bowel disease.

II. Diagnosis of Pulmonary Embolism

A. Signs and Symptoms of Pulmonary Embolism: Pleuritic chest pain, shortness of breath, tachycardia, hypoxemia, hypotension, hemoptysis, cough, syncope.

B. Classic triad of dyspnea, chest pain, and hemoptysis is seen in 20% of patients; the majority of patients have only a few subtle or ambiguous symptoms. Most pulmonary emboli are clinically inapparent or completely asymptomatic.

C. A deep venous thrombosis may be indicated by an edematous limb with an erythrocyanotic appearance, dilated superficial veins, and elevated

skin temperature.

D. The best diagnostic approach to pulmonary embolism is to search for an alternative diagnosis that can be more readily proved. If this is accomplished, the workup for pulmonary embolism can be ended. However, if no other satisfactory explanation can be found in a patient with findings suggestive of pulmonary embolism, the workup must be pursued to completion.

III. Diagnostic Evaluation

A. Chest Films are nonspecific and insensitive for pulmonary embolism. The chest film may be normal, or it may show an elevated hemidiaphragm, focal infiltrates, large or small pleural effusions, or atelectasis.

B. Electrocardiogram abnormalities are nonspecific. The tracing is often normal; the most commonly seen abnormality is sinus tachycardia. Occasionally, acute right ventricular strain causes tall and peaked P waves in lead II, right axis deviation, right bundle branch block, a classic S1-Q3-T pattern, or atrial fibrillation.

C. Blood Gas Studies

1. There is no level of arterial oxygen that can rule out pulmonary embolism. Most patients with pulmonary embolism have a normal arterial oxygen. Impaired gas exchange is best assessed by using the room air, alveolar-to-arterial (A-a) oxygen gradient:

A-a oxygen gradient = 147 - [1.2 (PCO_2) + measured pAO_2]

2. A normal gradient should be no higher than 10 plus one tenth of the patient's age.

3. A normal A-a oxygen gradient is seen in 5-15% of patients with pulmonary emboli but is inconsistent with massive pulmonary embolism and hypotension. An elevated gradient is nonspecific and may be produced by almost any pulmonary disease.

D. Ventilation-perfusion Scan: Virtually all patients suspected of having pulmonary emboli need a V/Q scan. Unfortunately, the V/Q scan is most often nondiagnostic; patterns other than "normal" and "high-probability" are nondiagnostic. Pulmonary angiography is necessary when the V/Q scan is nondiagnostic.

E. Venous Imaging

1. If the V/Q scan is nondiagnostic, a workup for deep venous thrombosis (DVT) should be pursued using duplex ultrasound and impedance plethysmography. The identification of DVT in a patient with signs and symptoms suggesting pulmonary embolism proves the diagnosis of pulmonary embolism.

2. Inability to demonstrate a source of DVT does not significantly lower the likelihood of pulmonary embolism because clinically asymptomatic DVT may not be detectable.

3. Patients with a nondiagnostic V/Q scan and no demonstrable site of DVT should proceed to pulmonary angiography.

F. Angiography

1. Contrast pulmonary arteriography is the "gold standard" for the diagnosis of pulmonary embolism, with unmatched sensitivity and specificity.

2. False-negative results occur in 2-10% of patients. False-positive results are extremely rare.

IV. Management of Acute Pulmonary Embolism in Stable Patients

A. Intravenous access and oxygen should be initiated for all patients.

B. Heparin Anticoagulation

1. In the absence of specific contraindications, heparin therapy should be started as soon as the diagnosis of pulmonary embolism is suspected. Full anticoagulating doses of heparin can be given immediately after major surgery.

2. Heparin IV bolus 5000-10,000 U (100 U/kg) then 1000-2000 U/h (20 U/kg/h) [25,000 U in 250 mL D5W (100 U/mL)]; adjust q6h to PTT 1.5-2.5 times control (55-85 sec). Draw PTT 6 hours after bolus and q6h until PTT 1.5-2.5 times control, then qd or q12h.

3. Heparin dosing for pulmonary embolism is the same as that for deep venous thrombosis.

4. Check activated partial thromboplastin time (PTT) 6 hours after therapy is initiated or after the dosage is adjusted.

Maintenance Dose Adjustment

aPTT	Hold Drip	Adjust Drip	Check aPTT
<50 sec	0 min	Increase by 200 U/h	6 hr later
50-55 sec	0 min	Increase by 150 U/h	6 hr later
55-85 sec	0 min	No change	Next morning
86-95 sec	0 min	Decrease by 100 U/h	Next morning
96-120 sec	30 min	Decrease by 150 U/h	6 hr later
>120 sec	60 min	Decrease by 200 U/h	6 hr later

5. Heparin should be continued for a 5-day course (including 4 days of overlap with warfarin).

6. Monitor platelet count during heparin therapy; thrombocytopenia develops in up to 5%. Heparin rarely induces hyperkalemia, which resolves spontaneously upon discontinuation.

7. After full anticoagulation has been established with heparin (within 24 hours), oral warfarin (Coumadin) may be initiated. It is not safe to start warfarin without prior heparinization, because the drug causes a hypercoagulable state during the early stages of its use. Ambulation can begin once the PTT is in the therapeutic range.

C. Warfarin (Coumadin) Therapy

1. Initial dose of warfarin is 5-10 mg for 2-3 days; subsequent doses should be based on a daily INR value and its rate of change. The dosage is typically 2-7.5 mg PO qd.

2. Administration of heparin and warfarin should overlap for a minimum of 3-5 days. Once heparin therapy has overlapped with warfarin therapy for 3-5 days and the INR is 2.0-3.0, heparin can be safely discontinued.

3. Length of Warfarin Therapy: If risk factors (prolonged inactivity) have been corrected, a 3-6 month course of warfarin is sufficient.

Persistent risk factors, extensive or complicated thrombosis, or recurrent thrombotic episodes may be indications to prolong therapy to 6-12 months. Outpatients receiving oral anticoagulants should have their INR checked weekly.

V. Management of Acute Pulmonary Embolism in Unstable Condition

A. Patients with pulmonary embolism who have severe hypoxemia or any degree of hypotension are considered to be in unstable condition.

B. Heparin and oxygen should be started immediately.

C. Fluid and Pharmacologic Management

1. In most cases of acute cor pulmonale, gentle pharmacologic preload reduction unloads the congested pulmonary circuit and reduces right ventricular pressures.

2. Hydralazine, isoproterenol, or norepinephrine may be required.

3. Pulmonary artery pressure monitoring is essential.

D. Thrombolysis and Embolectomy

1. Unstable patients (systolic <90 mmHg) with proven pulmonary embolism require immediate clot removal by thrombolytic therapy or by emergency surgical embolectomy. The benefits of intervention far outweigh any relative contraindications.

2. Full dose heparin should always be started immediately after the infusion of any thrombolytic agent.

3. Thrombolytic therapy usually is indicated only when the diagnosis of pulmonary embolism has been proved beyond a reasonable doubt. However, it may be impossible to prove the diagnosis rapidly enough to save the life of a patient in unstable condition, and thrombolysis should be attempted as a last-ditch effort in an otherwise moribund patient with a diagnosis of suspected massive pulmonary embolism.

4. The fastest-acting thrombolytic agent available, tissue plasminogen activator (Activase), should be used.

5. Contraindications to Thrombolytics

a. Absolute Contraindications: Active bleeding, recent stroke, central nervous system tumor.

b. Relative Contraindications: Surgical procedure within preceding 10 days; recent gastrointestinal bleeding; uncontrolled hypertension; recent trauma (cardiopulmonary resuscitation), pregnancy.

6. Advanced age, menstruation, and controlled hypertension are not contraindications to thrombolysis or heparin.

7. Monitor complete blood count, INR, activated PTT, and fibrinogen levels twice daily.

8. Alteplase (tPA, Activase): total dose of 100 mg is given over period of 2 hours.

9. Streptokinase

a. The period required for clot lysis is substantially longer with streptokinase than with tissue plasminogen activator.

b. Baseline CBC, PT/PTT, fibrinogen, thrombin time, UA; acetaminophen, methylprednisolone 250 mg IV, diphenhydramine are given.

c. Bolus of 250,000 units IV over 30 min, then 100,000 units/h for 24 hours.

VI. Emergency Thoracotomy

A. Emergency surgical removal of embolized thrombus is reserved for instances when there is an absolute contraindication to thrombolysis or when the patient's condition has failed to improve after thrombolysis.

B. Cardiac arrest from pulmonary embolism is an indication for immediate thoracotomy.

Asthma

Labs: ABG, CBC, SMA7, phosphate, theophylline level. CXR, pulmonary function test with bronchodilators, ECG.

Treatment:

-Oxygen 2-6 L/min by NC. Keeping SaO_2 >90%. Monitor pulse oximeter and peak flow rate before and after bronchodilator treatments.

Beta Agonists:

-Beta Agonists are the mainstay of treatment of acute and chronic asthma.

-Albuterol (Ventolin, Proventil)l nebulized, 0.5 mL (2.5 mg) in 3 mL saline initially, then q2-6h prn (5 mg/mL sln) **OR**

-Albuterol (Ventolin, Proventil) or Metaproterenol (Alupent) up to 20 puffs over a 10-20 min treatment period, repeated every 20-30 min prn. Then 2 puffs q1-6h prn or powder 200 mcg/capsule inhaled qid prn **OR**

-Pirbuterol (Maxair) MDI 2 puffs qid prn.

-Salmeterol (Serevent) 2 puffs bid; beneficial for prophylaxis of exercise-induced and nocturnal asthma; not for acute asthma because of slow onset of action.

Corticosteroids and Ipratropium:

-Methylprednisolone (Solu-Medrol) 40-125 mg IV q6h; then 30-60 mg PO qd.

-Prednisone 40-60 mg PO qAM.

-Beclomethasone (Beclovent, Vanceril) 2-6 puffs qid, with spacer 5 min after bronchodilator, followed by gargling with water.

-Triamcinolone (Azmacort) 1-4 puffs tid-qid.

-Budesonide (Pulmicort) 2-4 puffs bid-qid.

-Fluticasone (Flovent) 2-4 puffs bid. 1-2 weeks required for full effect.

-Albuterol and ipratropium (Combivent) 2-4 puffs qid.

Leukotriene Receptor Antagonist:

-Zafirlukast (Accolate) 20 mg PO bid on an empty stomach. Effective in prevention and treatment of acute/chronic asthma. Marked prolongation of prothrombin time occurs when taken with warfarin.

Aminophylline and Theophylline:

-Aminophylline loading dose: 5.6 mg/kg **total** body weight in 100 mL D5W IV over 20-30 min. Maintenance of 0.5-0.6 mg/kg (**ideal** body weight)/h (500 mg in 250 mL D5W); reduce if elderly, heart/liver failure (0.2-0.4 mg/kg/hr). Reduce load by 50-75% if taking theophylline (1 mg/kg of aminophylline will raise levels 2 µg/mL) **OR**

-Theophylline IV solution loading dose 4.5 mg/kg **total** body weight, then 0.4-0.5 mg/kg (**ideal** body weight)/hr.

-Theophylline (Theo-Dur) PO loading dose of 6 mg/kg, then maintenance of 100-400 mg PO bid-tid (3 mg/kg q8h); 80% of total daily IV aminophylline in 2-3 doses.

Symptomatic Medications:
-Docusate sodium (Colace) 100-200 mg PO qhs.
-Ranitidine (Zantac) 50 mg IV q8h or 150 mg PO bid.

Chronic Obstructive Pulmonary Disease

Labs: ABG, CBC, phosphate, SMA7, UA. Theophylline level. Sputum Gram stain and C&S. CXR, PFT's with bronchodilators, ECG, PPD with controls. Peak flow rate pre & post bronchodilators, pulse oximeter.
Treatment:
-O_2 1-2 L/min by NC or 24-35% by Venturi mask, keep O_2 saturation 90-91%. Use oxygen cautiously if chronic hypercapnia.
Acute Beta-Agonist Therapy:
-Nebulized Albuterol (Ventolin, Proventil) or 0.5 mL in 3 mL (2.5 mg) of saline [with unit dose of ipratropium] initially, then q2-8h prn (5 mg/mL sln) **OR**
-Albuterol (Ventolin, Proventil) 2-8 puffs then 2 puffs; then 2 puffs q4-6h prn; add ipratropium (Atrovent), 2-4 puffs q4-6h.
-Albuterol and ipratropium (Combivent) 2-4 puffs qid.
Aminophylline and Theophylline:
-Aminophylline loading dose-5.6 mg/kg **total** body weight over 20-30 min; then 0.5-0.6 mg/kg (**ideal** body weight)/hr (500 mg in 250 mL of D5W); reduce if elderly, heart or liver disease (0.2-0.4 mg/kg/hr). Reduce loading by 50-75% if already taking theophylline (1 mg/kg of aminophylline will raise level by 2 µg/mL) **OR**
-Theophylline IV solution loading dose 4.5 mg/kg **total** body weight, then 0.4-0.5 mg/kg (**ideal** body weight)/hr.
-Theophylline long acting (Theo-Dur) PO loading dose of 6 mg/kg, then maintenance of 100-400 mg PO bid-tid (3 mg/kg q8h); 80% of daily IV aminophylline in 2-3 doses.
Corticosteroids and Anticholinergics:
-Methylprednisolone (Solu-Medrol) 40-60 mg IV q6h or 30-60 mg PO qd **OR**
-Prednisone 40-60 mg PO qd, taper to minimum dose.
-Triamcinolone (Azmacort) 2-4 puffs qid **OR**
-Beclomethasone (Beclovent) 2-6 puffs qid, with spacer, 5 min after bronchodilator, followed by gargling with water
-Flunisolide (Aerobid) 2-4 puffs bid **OR**
-Fluticasone (Flovent) 2-4 puffs bid. Full effect requires 1-2 weeks.
-Ipratropium Bromide (Atrovent) 2 puffs tid-qid.
Acute Bronchitis:
-Ampicillin 1 gm IV q6h or 250-500 mg PO qid **OR**
-Trimethoprim/Sulfamethoxazole (Septra DS) 160/800 mg PO bid or 10 mL of IV solution in 100 mL D5W IVPB q8-12h [80/400 mg/5 mL] **OR**
-Ampicillin/sulbactam (Unasyn) 1.5 gm IV q6h
-Cefuroxime (Zinacef) 0.75-1.5 gm IV q8h **OR**
-Clarithromycin (Biaxin) 250-500 mg PO bid [250, 500 mg].
Symptomatic Medications:
-Docusate sodium (Colace) 100-200 mg PO qhs.
-Ranitidine (Zantac) 50 mg IV q8h or 150 mg PO bid.

Pleural Effusion

Labs: CBC, ABG, SMA 12, protein, albumin, amylase, rheumatoid factor, ANA, ESR, PT/PTT, UA. CXR PA & LAT repeat after thoracentesis, bilateral decubitus, ECG, ultrasound.

Pleural fluid:

Tube 1-LDH, protein, amylase, triglyceride, glucose, (10 mL).

Tube 2-Gram stain, C&S, AFB, fungal C&S, wet mount (20-60 mL, heparinized).

Tube 3-Cell count and differential (5-10 mL, EDTA).

Tube 4-Sudan stain, LE prep, antigen tests for S pneumoniae, H influenza (25-50 mL, heparinized).

Syringe-pH (2 mL collected anaerobically, heparinized on ice)

Bag or Bottle-cytology.

Evaluation of Pleural Fluid

Pleural Fluid Parameter	Transudate	Exudate
Pleural fluid protein/serum protein	<0.5	>0.5
Pleural fluid LDH	<200	>200
Pleural fluid LDH/serum LDH	<0.6	>0.6

Differential Diagnosis:

Transudate: Congestive heart failure, cirrhosis.

Exudate: Empyema, viral pleuritis, tuberculosis, neoplasm, uremia, drug reaction, asbestosis, sarcoidosis, collagen disease (lupus, rheumatoid disease), pancreatitis, subphrenic abscess.

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Trauma

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Pneumothorax

I. Management of Pneumothorax

A. Small Primary Spontaneous Pneumothorax (<10-15%): (not associated with underlying pulmonary diseases). If the patient is Not Dyspneic

1. Observe for 4-8 hours and repeat a chest X-ray.

2. If the pneumothorax does not increase in size and the patient remains asymptomatic, consider discharge home with instructions to rest and curtail all strenuous activities. Return if increase in dyspnea or recurrence of chest pain.

B. Secondary Spontaneous Pneumothorax (associated with underlying pulmonary pathology, most commonly emphysema) or Primary Spontaneous Pneumothorax >15%, or if patient is symptomatic

1. Give high flow oxygen. A needle thoracotomy should be placed at the anterior, second intercostal space in the midclavicular line.

2. Anesthetize and prep the area, then insert a 16-gauge needle with an internal catheter and a 60 mL syringe attached via a 3-way stopcock. Aspirate until no more air is aspirated. If no additional air can be aspirated, and the volume of aspirated air is <4 liters, occlude the catheter and observe for 4 hours.

3. If symptoms abate and chest-x-ray does not show recurrence of the pneumothorax: the catheter can be removed, and the patient can be discharged home with instructions.

4. If the aspirated air is >4 liters and additional air is aspirated without resistance, this represents an active bronchopleural fistula with continued air leak. Admission is required for insertion of a chest tube.

C. Traumatic Pneumothorax associated with a penetrating injury, hemothorax, mechanical ventilation, tension pneumothorax, or if pneumothorax does not resolve after needle aspiration: Give high flow oxygen and insert a chest tube, along with aggressive hemodynamic and respiratory resuscitation as indicated. Do not delay the management of a tension pneumothorax until radiographic confirmation, insert needle thoracotomy or chest tube immediately.

II. Technique of Chest Tube Insertion

A. Place patient in supine position, with involved side elevated 20 degrees; abduct arm at 90 degrees. The usual site is the fourth or fifth intercostal space, between the mid-axillary and anterior axillary line (drainage of air or free fluid). The point at which the anterior axillary fold meets the chest wall is a useful guide. Consult the chest radiograph for further guidance if time permits. Alternatively, the second or third intercostal space, in the mid-clavicular line, may be used for

pneumothorax drainage alone (air only).

B. Cleanse skin with Betadine iodine solution and drape the field. Determine the intrathoracic tube distance (lateral chest wall to the apices), and mark the length of tube with a clamp.

C. Infiltrate 1% lidocaine into the skin, subcutaneous tissues, intercostal muscles, periosteum, and pleura using a 25-gauge needle. Use a scalpel to make a transverse skin incision, 2 centimeters wide, located over the rib just inferior to the interspace where the tube will penetrate the chest wall.

D. Using a Kelly clamp to bluntly dissect a subcutaneous tunnel from the skin incision, extending just over the superior margin of the lower rib. Avoid the nerve, artery and vein located at the upper margin of the intercostal space.

E. Penetrate the pleura with the clamp, and open the pleura 1 centimeter.

F. With a gloved finger, explore the subcutaneous tunnel, and palpate the lung medially. Exclude possible abdominal penetration, and ensure correct location within pleural space; use finger to remove any local pleural adhesions.

G. Use the Kelly clamp to grasp the tip of the thoracostomy tube (36 F, internal diameter 12 mm), and direct it into the pleural space in a posterior, superior direction for pneumothorax evacuation. Direct tube inferiorly for pleural fluid removal. Guide the tube into the pleural space until the last hole is inside the pleural space and not inside the subcutaneous tissue.

H. Attach the tube to a underwater seal apparatus containing sterile normal saline, and adjust to 20 cm H_2O of negative pressure, or attach to suction if leak is severe. Suture the tube to the skin of the chest wall using O silk. Apply Vaseline gauze, 4 x 4 gauze sponges, and elastic tape. Obtain a chest X-ray to verify correct placement and evaluate reexpansion of lung.

Tension Pneumothorax

I. Clinical Evaluation

A. Clinical Signs: Severe hemodynamic and/or respiratory compromise; contralaterally deviated trachea; decreased or absent breath sounds and hyperresonance to percussion on the affected side; jugular venous distention, asymmetrical chest wall motion with respiration.

B. Radiologic Signs: Flattening or inversion of the ipsilateral hemidiaphragm; contralateral shifting of the mediastinum; flattening of the cardio-mediastinal contour and spreading of the ribs on the ipsilateral side.

II. Acute Management

A. A temporary large-bore IV catheter may be inserted into the ipsilateral pleural space, at the level of the second intercostal space at the mid-clavicular line until the chest tube is placed.

B. A chest tube should be placed emergently.

C. Draw blood for CBC, INR, PTT, type and cross-matching, Chem 7, Toxicology screen.

D. Send pleural fluid for hematocrit, amylase and pH (to rule out possible

esophageal rupture).

E. Indications for Cardiothoracic Exploration: Penetrating chest injury, persistent air leak, severe or persistent hemodynamic instability despite aggressive fluid resuscitation, persistent active blood loss from chest tube.

Cardiac Tamponade

I. General Considerations

A. Cardiac tamponade occurs most commonly secondary to penetrating injuries.

B. Beck's Triad: Venous pressure elevation, drop in the arterial pressure, muffled heart sounds.

C. Other Signs: Enlarged cardiac silhouette on CXR; signs and symptoms of hypovolemic shock; electromechanical dissociation (pulseless electrical activity), decreased voltage on ECG.

D. Kussmaul's sign is characterized by a rise in venous pressure with inspiration. Pulsus paradoxus or elevated venous pressure may be absent when associated with hypovolemia.

II. Management

A. Pericardiocentesis is indicated if patient is unresponsive to the usual resuscitation measures for hypovolemic shock, or if there is a high likelihood of injury to the myocardium or one of the great vessels.

B. All patients who have a positive pericardiocentesis (recovery of non-clotting blood) because of trauma, require an open thoracotomy with inspection of the myocardium and the great vessels.

C. Rule out other causes of cardiac tamponade such as pericarditis, penetration of central line through the vena cava, atrium, or ventricle, or infection.

D. Consider other causes of hemodynamic instability that may mimic cardiac tamponade (tension pneumothorax, massive pulmonary embolism, shock secondary to massive hemothorax).

Pericardiocentesis

I. General Considerations

A. If acute cardiac tamponade with hemodynamic instability is suspected, emergency pericardiocentesis should be performed; infusion of Ringer's lactate, crystalloid, colloid and/or blood may provide temporizing measures.

II. Management

A. Protect airway and administer oxygen. If patient can be stabilized, pericardiocentesis should be performed by a specialist in the operating room or catheter lab. The para-xiphoid approach is used for pericardiocentesis.

B. Place patient in supine position with chest elevated at 30-45 degrees, then cleanse and drape peri-xiphoid area. Infiltrate lidocaine 1% with epinephrine (if time permits) into skin and deep tissues.

C. **Attach a long, large bore (12-18 cm, 16-18 gauge), short bevel cardiac needle** to a 50 cc syringe with a 3-way stop cock. Use a alligator clip to attach a V-lead of the ECG to the metal of the needle.

D. **Advance the needle** just below costal margin, immediately to the left and inferior to the xiphoid process. Apply suction to the syringe while advancing the needle slowly at a 45 degree horizontal angle towards the mid point of the left clavicle.

E. **As the needle penetrates** the pericardium, resistance will be felt, and a characteristic "popping" sensation will be noted.

F. **Monitor the ECG** for ST segment elevation (indicating ventricular heart muscle contact); or PR segment elevation (indicating atrial epicardial contact). After the needle comes in contact with the epicardium, withdraw the needle slightly. Ectopic ventricular beats are associated with cardiac penetration.

G. Aspirate as much blood as possible. Blood from the pericardial space usually will not clot. Blood, inadvertently, drawn from inside the ventricles or atrium usually will clot. If fluid is not obtained, redirect the needle more towards the head.

H. Stabilize the needle by attaching a hemostat or Kelly clamp.

I. Consider emergency thoracotomy to determine the cause of hemopericardium (especially if active bleeding). If the patient does not improve, consider other problems that may resemble tamponade, such as tension pneumothorax, pulmonary embolism, or shock secondary to massive hemothorax.

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Hematology

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Transfusion Reactions

I. Acute Hemolytic Transfusion Reaction

A. Clinical Presentation: This rare reaction is most commonly associated with ABO incompatibility, and it is usually related to a clerical error. Early symptoms include sudden onset of anxiety, flushing, tachycardia, and hypotension. Chest and back pain, fever and dyspnea are common.

B. Life threatening manifestations include vascular collapse (shock), renal failure, bronchospasm, and disseminated intravascular coagulation.

C. Hemoglobinuria, and hemoglobinemia occurs because of intravascular red cell lysis.

D. A positive direct antiglobulin test (direct Coombs test) will be found after transfusion. The severity of reaction is usually related to the volume of RBC's infused.

E. Management

1. Discontinue transfusion and notify blood bank immediately. Send the unused donor blood and a sample of recipient's venous blood for retyping and repeat cross match including direct and indirect Coombs test.

2. Check urine analysis for free hemoglobin and check centrifuged plasma for pink coloration (indicating free hemoglobin).

3. Manage hypotension with normal saline or plasma expanders. Vasopressors may be used if volume replacement alone is inadequate to maintain blood pressure. Central venous monitoring may be necessary.

4. Maintain adequate renal perfusion with volume replacement. Mannitol and/or furosemide may be used to maintain urine output after adequate volume replacement has been achieved.

5. Monitor PT/PTT, platelets, fibrinogen, and fibrin degradation products for evidence of disseminated intravascular coagulation. Replace required clotting factors with fresh frozen plasma, platelets, and/or cryoprecipitate.

6. In rare circumstances, exchange transfusions have been performed for massive intravascular hemolysis.

II. Febrile Transfusion Reaction (nonhemolytic)

A. Clinical Presentation: This reaction occurs in 0.5-3% of transfusions, and is most commonly seen in patients receiving multiple transfusions. Chills develop followed by fever, usually during or within a few hours of transfusion. This reaction may be severe but is usually mild and self limited.

B. Management

1. Provide symptomatic and supportive care with acetaminophen and diphenhydramine. Meperidine 50 mg IV is useful in treating chills.

2. More serious transfusion reactions must be excluded (eg, acute hemolytic reaction or bacterial contamination of donor blood).

III. Transfusion Related Noncardiogenic Pulmonary Edema

A. Clinical Presentation is characterized by sudden development of severe respiratory distress, associated with fever, chills, chest pain, and hypotension.

B. Chest radiograph demonstrates diffuse pulmonary edema. This reaction may be severe and life threatening but generally resolves within 48 hours.

C. Management

1. Provide supportive measures for pulmonary edema and hypoxemia including mechanical ventilatory support and hemodynamic monitoring if needed.

2. Diuretics are useful only if fluid overload is present.

Disseminated Intravascular Coagulation

I. Clinical Manifestations

A. DIC is manifest by generalized ecchymosis and petechiae, bleeding from peripheral IV sites, central catheters, surgical wounds, and oozing from gums.

B. Gastrointestinal and urinary tract bleeding are frequently encountered. Grayish discoloration or cyanosis of the distal fingers, toes, or ears may occur because of intravascular thrombosis.

C. Large, sharply demarcated ecchymotic areas may be seen as a result of thrombosis of the dermal blood supply.

II. Diagnosis

A. Fibrin degradation products are the most sensitive screening test for DIC; however, no single laboratory parameter is diagnostic of DIC, and findings may be quite variable. Repeated testing of coagulation parameters may provide a kinetic assessment of the rate and degree of factor consumption or replacement.

B. Peripheral Smear: Evidence of microangiopathic hemolysis with schistocytes and thrombocytopenia are present. A persistently normal platelet count nearly excludes the diagnosis of acute DIC.

C. Coagulation Studies: INR, PTT, and thrombin time are generally prolonged. Fibrinogen levels are usually depleted (<150 mg/dL). Fibrin degradation products are elevated (>10 mg/dL). D-dimer is elevated (>0.5 mg/dL).

III. Management of Disseminated Intravascular Coagulation

A. The primary underlying precipitating condition (eg, sepsis) is treated. Reversal of the syndrome depends on the treatment of the underlying disorder.

B. Severe DIC with hypocoagulability may be treated with replacement of clotting factors; hypercoagulability is managed with inhibition of coagulation with heparin.

C. Severe hemorrhage and shock is managed with fluids and red blood cell transfusions.

D. If the Patient is at High Risk of Bleeding or Actively Bleeding with Biochemical Evidence of DIC: Replace fibrinogen with 10 units of cryoprecipitate. Replace clotting factors with 2-4 units of fresh frozen plasma. Replace platelets with platelet phoresis.

E. If Factor Replacement Therapy Is Transfused, fibrinogen and platelet levels should be obtained 30-60 minutes post-transfusion and every 4-6 hours thereafter to determine the efficacy of therapy. Each unit of platelets should increase the platelet count by 5000-10,000/mcL. Each unit of cryoprecipitate should increase fibrinogen level by 5-10 mg/dL.

F. Heparin:

1. The use of heparin is controversial. Indications for heparin include evidence of fibrin deposition (i.e. dermal necrosis, acral ischemia, venous thromboembolism).

2. Heparin is used when the coagulopathy is believed to be secondary to a retained dead fetus, amniotic fluid embolus, giant hemangiomas, aortic aneurysm, solid tumors, or promyelocytic leukemia. Heparin is also used when clotting factors cannot be corrected with replacement therapy alone.

3. Heparin therapy is initiated at a relatively low dose (5-10 U/kg/hr) by continuous IV infusion without bolus. Coagulation parameters must then be followed to guide therapy. If desired increments of clotting factors do not occur, the heparin dose may be increased by 2.5 U/kg/hr until the desired effect is achieved.

Thrombolytic Associated Bleeding

I. Clinical Presentation: Post-fibrinolysis hemorrhage has varied presentations, including sudden neurologic deficit (intracranial bleeding), massive volume loss (as in GI bleeding), or gradual decline in hemoglobin without overt evidence of bleeding.

II. Laboratory Evaluation

A. Elevated thrombin time and PTT identify a persistent lytic state; however, both are prolonged in the presence of heparin.

B. Prolonged reptilase time identifies the persistent lytic state in the presence of heparin.

C. Depleted fibrinogen in the fibrinolytic state will be reflected by an elevated PTT, thrombin time, or reptilase time. The post-transfusion fibrinogen level is a useful indicator of response to replacement therapy.

D. Elevated fibrin degradation products confirm the presence of a lytic state.

E. The bleeding time, as an indicator of platelet function, may be a helpful guide to platelet replacement therapy if the patient has persistent bleeding despite factor replacement with cryoprecipitate, and fresh frozen plasma.

III. Management

A. Discontinue thrombolytics, aspirin, and heparin immediately, and consider protamine reversal of heparin.

B. Place two large bore IV catheters for volume replacement. If possible, apply local pressure to bleeding sites.

C. Send blood specimens for INR/PTT, fibrinogen, and thrombin time. Check reptilase time if patient is also receiving heparin.

D. Patient's blood should be typed and crossed because urgent transfusion may be needed.

E. Transfusion

1. Cryoprecipitate (10 units over 10 minutes) should be transfused as a first-line measure to correct the lytic state. Transfusions may be repeated until the fibrinogen level is above 100 mg/dL or hemostasis is achieved.
2. Fresh frozen plasma transfusion is also important for replacement of factor VIII and V. If bleeding persists after cryoprecipitate and FFP replacement, check a bleeding time and consider platelet transfusion if bleeding time is greater than 9 minutes. If bleeding time is less than 9 minutes, then antifibrinolytic drugs may be warranted.

F. Antifibrinolytic Agents

1. Aminocaproic acid (EACA) inhibits the binding of plasmin to fibrin and plasminogen to fibrinogen. It is used when replacement of blood products are not sufficient to attain hemostasis; potential risk of serious thrombotic complications.
2. Loading dose: 5 g or 0.1 g/kg IV infused in 250 cc NS over 30-60 min, followed by continuous infusion at 0.5 to 1.0 g/h until bleeding is controlled. Use with caution in upper urinary tract bleeding because of the potential for obstruction. Contraindicated in DIC.

G. If Bleeding Is Suspected on the Basis of Falling Hemoglobin Without Overt Evidence of Blood Loss: Occult sources must be considered, including the retroperitoneal space, thigh (often related to femoral venous or arterial puncture), bleeding into other body cavities (peritoneum, thorax).

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Infectious Diseases

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Empiric Therapy of Meningitis

I. Labs: CBC, SMA 12, blood C&S x 2. UA, urine C&S. Antibiotic levels peak and trough after 3rd dose.

CSF Tube 1-Gram stain of fluid or sediment (if fluid is clear), C&S for bacteria (1-4 mL).

CSF Tube 2-Cell count and differential (1-2 mL).

CSF Tube 3-Glucose, protein (1-2 mL).

CSF Tube 4-Latex agglutination or counterimmunoelectrophoresis antigen tests for S. pneumoniae, H. influenzae (type B), N. meningitides, E. coli, group B strep, cryptococcus, viral cultures, VDRL (8-10 mL).

Other Tests: CXR, ECG.

II. Treatment:

A. If mass lesion is not suspected: Complete lumbar puncture, then initiate antibiotics.

B. If mass lesion suspected, initiate antibiotics before CT scan or MRI; perform lumbar puncture if no signs of elevated intracranial pressure are apparent.

C. Meningitis Empiric Therapy

-Ampicillin 2 gm IV q4h (with 3rd gen cephalosporin) **AND EITHER**
Ceftriaxone (Rocephin) 2 gm IV q12h (max 4 gm/d) **OR**
Cefotaxime (Claforan) 2 gm IV q4h.

-Vancomycin, children: 15 mg/kg IV q6h; adults: 1.0 gm IV q12h. Vancomycin is added if there is a high prevalence of drug resistant Streptococcus pneumoniae in the community.

-Consider dexamethasone IV if increased intracranial pressure or significant CNS dysfunction.

D. Meningitis After Neurosurgical Procedures or Craniospinal Trauma:

-Vancomycin 1 gm IV q12h **AND**
-Ceftazidime (Fortaz) 2 gm IV q8h, max 12 g/d.

Cerebral Spinal Fluid Analysis

Disease	Color	Protein	Cells	Glucose
Normal CSF Fluid	Clear	<50 mg/100 mL	<5 lymphs/ mm^3	>40 mg/100 mL, 1/2-2/3 blood sugar drawn at same time
Bacterial meningitis early viral or tuberculous meningitis	Yellow opales-cent	Elevated 50-1500	25-10000 WBC with predomin-ate polys	low

Tuberculous, fungal, partially treated bacterial, syphilitic meningitis, meningeal metastases	Clear opales-cent	Elevated usually <500	10-500 WBC with predomin-ant lymphs	20-40, low
Viral meningitis, partially treated bacterial meningitis, encephalitis, toxoplasmosis, parameningeal infection	Clear opales-cent	Slightly elevated or normal	10-500 WBC with predomina nt lymphs	normal, may be low

Pneumonia

Pneumonia remains a common cause of death. Streptococcus pneumoniae is the most common etiologic agent identified, however, many bacteria, viruses, and fungi can cause pneumonia.

I. Clinical Evaluation

A. Pneumonia typically manifest with cough productive of yellow-green, even blood-streaked sputum; dyspnea, pleuritic chest pain, fevers (often spiking to 104° F), chills, and shaking rigors are common.

B. The chest examination reveals consolidation, including an area of dullness to percussion, and increased breath sounds (bronchial type).

C. The organisms that cause typical pneumonias are usually the bacterial pathogens Streptococcus pneumoniae and Hemophilus influenzae.

D. Chest Radiography is useful for differentiating bronchitis.

1. If no infiltrate is seen on x-ray, pneumonia is virtually excluded, even for dehydrated, elderly patients. Infiltrates may not be detected in 10-15% of AIDS patients with P carinii pneumonia.

E. Gram's Stain and Culture

1. Squamous epithelial cells in large numbers suggests that the specimen is contaminated with upper respiratory secretions; the specimen should have <10 squamous epithelial cells per low power field. WBC's indicate a lower respiratory source of sputum.

2. Sputum culture reports should always be interpreted in light of the Gram stain results.

F. Blood Cultures can occasionally provide additional diagnostic information in hospitalized patients, particularly in HIV infected patients.

G. Specialized Tests:

1. Acid-fast stain and culture for tuberculosis.

2. Specific tests for Legionella pneumophila, fungi, viruses

3. Serologic tests: Complement fixation (M pneumoniae), ELISA (IgM and IgA) for M pneumoniae.

4. Indirect fluorescent antibody test (L pneumophila); microimmunofluorescence (Chlamydia pneumoniae).

II. Inpatient Management of Pneumonia

A. Hospitalized Patients with Community-Acquired Pneumonia should receive a second or third-generation cephalosporin or beta-lactam/beta-lactamase inhibitor (ampicillin/sulbactam) plus erythromycin. If methicillin-resistant S aureus is prevalent, vancomycin may be added.

B. The beta-lactamase inhibitor combinations, ampicillin/sulbactam (Unasyn) or ticarcillin clavulanate (Timentin), provide excellent coverage for anaerobes as well as traditional bacterial pathogens.

1. Ampicillin/Sulbactam (Unasyn) 1.5 gm IV q6h **OR**
2. Ticarcillin/clavulanate (Timentin) 3.1 gm IV q4-6h (200-300 mg/kg/d) **OR**
3. Piperacillin/Tazobactam (Zosyn) 3.375 gm IV q6h **AND**
4. Erythromycin 500 mg IV q6h.
5. Cefuroxime (Zinacef) 1.5 gm IV q8h **OR**
6. Cefotaxime (Claforan) 1-2 gm IV q8 **OR**
7. Ceftriaxone (Rocephin) 1-2 gm IV q12h **OR**
8. Ceftizoxime (Cefizox) 1-2 gm IV q8-12h **OR**
9. Trimethoprim/Sulfamethoxazole (Septra DS) 6-10 mg TMP/kg/d IV in 2-3 divided doses **OR**
10. Imipenem/cilastatin (Primaxin) 0.5-1.0 gm IV q6-8h.

Pneumocystis Carinii Pneumonia

The greatest risk for PCP occurs at a CD4 count of less than 200 cells/μL. There is a gradient of risk as the CD4 cell count decreases, with a small proportion of cases occurring at a CD4 higher then 200, and a greater risk of PCP at a CD4 below 100.

I. Diagnosis

A. Symptoms of PCP include progressive dyspnea, nonproductive cough, fever, night sweats and fatigue. A productive cough may sometimes be noted in PCP.

B. Diagnostic Procedures

1. **Chest x-ray** usually reveals diffuse, interstitial infiltrates; however, x-ray findings can often be normal or atypical.
2. **Induced Sputum Stain:** If performed properly, induced sputum examination can diagnose 85-95% of cases of PCP. Yield is improved with fluorescent monoclonal antibody stains. A negative sputum stain should be followed by a bronchoalveolar lavage to definitively rule out infection.
3. **Bronchoalveolar lavage (BAL)** should be performed in patients in whom the level of suspicion for PCP is high and in whom induced sputum examination is negative.
4. **Diffusion Capacity for Carbon Monoxide (DL_{CO})** may be useful for patients with a clinical suspicion for PCP who have a normal or atypical chest x-ray.
5. **High Resolution CT Scan:** Absence of typical changes (i.e. ground glass opacities) on this test may be useful to exclude PCP, but results may be falsely positive.

II. Treatment of Pneumocystis Carinii Pneumonia

A. Treatment for Mild to Moderate PCP Disease

1. Oral or IV trimethoprim/sulfamethoxazole (Bactrim, Septra); 15-20 mg/kg of the trimethoprim component daily in three divided doses (two double strength tabs tid) for 21 days. Alternative drugs may be used if treatment-limiting adverse effects occur or if there is failure to respond to TMP-SMX **OR**
2. Clindamycin 450 mg po tid plus primaquine 15 mg of base PO qd **OR**
3. Aerosolized pentamidine 300 mg/d **OR**
4. Atovaquone (Mepron) is used for mild to moderate PCP if the patient is able to take oral medication and there is no diarrhea; 750 mg PO tid for 21 days with food.
5. **Adjunctive corticosteroids** are recommended for patients with a room air A-a gradient $\geq$35 or a room air pO_2 <70 mm Hg; prednisone 40 mg po twice daily x 5 days, then 40 mg once daily for five days, then 20 mg once daily for the remainder of PCP therapy.

B. Treatment of Severe PCP Disease

1. IV trimethoprim/sulfamethoxazole 15 mg of trimethoprim component/kg/d in 3 divided doses (20 mL of IV solution in 100 mL of D5W IVPB q8h) [solution for injection: 80/400 mg/5 mL] **OR**
2. If the patient is intolerant or unresponsive to TMP-SMX, pentamidine (Pentam 300) IV may be used; 4 mg/kg IV infusion daily for 21 days. Nephrotoxicity and hypoglycemia are significant adverse effects **OR**
3. Clindamycin 600-900 mg IV q8h plus oral primaquine, 30 mg of base, PO qd is an alternative.

C. Steroids are used when the pO2 is <70 or the A-a gradient is greater than 35. Steroids should be started early (within 72 hours of the diagnosis).

1. Prednisone 40 mg PO bid x 5 days, then 20 mg PO bid x 5 days, then 20 mg qd to end of treatment **OR**
2. Methylprednisolone (Solu-Medrol) 40 mg IV q12h x 5 days, then 20 mg IV q12h, then 20 mg IV qd to end of treatment.

III. Pneumocystis Carinii Pneumonia Prophylaxis

A. CDC Criteria for Initiating Prophylactic Therapy

1. CD4 cell count less than 200 cells/μL
2. The percentage of CD4 cells is less than 20% of lymphocytes
3. A previous episode of PCP has occurred
4. Constitutional symptoms are present, such as thrush or unexplained fever >37.8°C for two or more weeks.

B. Prophylaxis is taken indefinitely, and is continued even if the CD4 count rises above 200 cells/μL.

C. **Trimethoprim/Sulfamethoxazole(Bactrim, Septra)** is the drug of choice; one double-strength tablet PO daily 3 times per week or one single-strength tab daily. TMP/SMZ is dually preventative against toxoplasmosis.

1. Patients taking TMP/SMZ therapy are monitored for leukopenia, anemia, thrombocytopenia, fever, rash (including Stevens-Johnson syndrome), azotemia, nausea, hepatitis, pruritus, and elevated transaminase levels.
2. Desensitization is often used if the drug reaction was mild.
3. Dapsone is an alternative agent; 50 mg PO bid or 100 mg twice a

week; contraindicated in G6PD deficiency.

D. Pentamidine (NebuPent) is another alternative agent; 300-mg (one vial in 6 mL sterile water) once a month via jet nebulizer (Respirgard II).

E. Alternative Prophylaxis Therapies

1. Pentamidine, 4 mg/kg once-monthly intramuscular or intravenous therapy: The data is scant, but this treatment may have possibly adequate efficacy. Monitor for pancreatitis in patients receiving concomitant DDI (Videx)

2. Dapsone-pyrimethamine: 200 mg/wk plus 25-75 mg/wk OR 50 mg/wk plus 50 mg/wk. This regimen is less effective than TMP-SMX; however, it may offer protection against toxoplasmosis in toxoplasma antibody-positive individuals.

Antiretroviral Therapy and Opportunistic Infections in AIDS

I. Antiretroviral Therapy

A. Combination therapy with a nucleoside analog and a protease inhibitor is the most effective regimen. Two nucleosides, or a nucleoside plus a protease inhibitor is superior to monotherapy with zidovudine.

B. Nucleoside Analogs

1. Zidovudine (Retrovir, AZT) 200 mg PO tid [cap: 100 mg, 200 mg].

2. Lamivudine (Epivir) 150 mg PO bid [tab: 150 mg].

3. Stavudine (Zerit) 40 mg PO bid [cap: 15, 20, 30, 40 mg].

4. Zalcitabine (Hivid) 0.75 mg PO tid [tab: 0.375, 0.75 mg].

5. Didanosine (Videx) 200 mg PO bid [chewable tabs: 25, 50, 100, 150 mg]; oral ulcers discourage common usage.

C. Protease Inhibitors:

1. Indinavir (Crixivan) 800 mg PO tid [cap: 200, 400 mg].

2. Ritonavir (Norvir) 600 mg PO bid [cap: 100 mg].

3. Saquinavir (Invirase) 600 mg PO tid [cap: 200 mg].

D. Antiretroviral therapy during trimethoprim-sulfamethoxazole therapy may increase the marrow suppressing effects of both drugs.

II. Oral Candidiasis:

A. Fluconazole (Diflucan) Acute: 100-200 mg po qd **OR**

B. Ketoconazole (Nizoral), acute: 400 mg po qd 1-2 weeks or until resolved **OR**

C. Clotrimazole (Mycelex) troches 10 mg dissolved slowly in mouth 5 times/d.

III. Candida Esophagitis:

A. Fluconazole 400 mg po qd x 14-21 days; higher dosages might be required **OR**

B. Ketoconazole 200 mg po bid.

IV. Primary or Recurrent Mucocutaneous HSV

A. Acyclovir (Zovirax), 200-400 mg po 5 times a day for 10 days, or 5 mg/kg IV q8h OR in cases of acyclovir resistance, foscarnet, 40 mg/kg IV q8h for 21 days.

V. Herpes Simplex Encephalitis:

A. Acyclovir 10 mg/kg IV q8h x 10-21 days.

VI. Herpes Varicella Zoster

- **A.** Acyclovir (Zovirax) 10 mg/kg IV over 60 min q8h **OR**
- **B.** Valacyclovir (Valtrex) 1000 mg PO tid x 7 days [caplet: 500 mg].

VII. Cytomegalovirus infections

- **A.** Ganciclovir (Cytovene) 5 mg/kg IV (dilute in 100 mLs D5W over 60 min) q12h x 14-21 days (concurrent use with zidovudine increases hematological toxicity).
- **B. Suppressive Treatment for CMV:** Ganciclovir 5 mg/kg IV qd, or 6 mg/kg IV 5 times/wk, or 1000 mg orally tid with food [cap: 250 mg].

VIII. Toxoplasmosis

- **A.** Pyrimethamine 200 mg PO loading dose, then 50-75 mg qd plus leucovorin calcium (folinic acid) 10-20 mg po qd for 6-8 weeks for acute therapy **AND**
- **B.** Sulfadiazine 1 to 1.5 g PO q6h or clindamycin 450 mg PO qid/600-900 mg IV q6h.
- **C. Suppressive Treatment for Toxoplasmosis:**
  - **1.** Pyrimethamine 25-50 mg PO qd with or without sulfadiazine 0.5-1.0 Gm PO q6h; and folinic acid 5-10 mg PO qd. **OR**
  - **2.** Pyrimethamine 50 mg PO qd; and clindamycin 300 mg PO q6h; and folinic acid 5-10 mg PO qd.

IX. Cryptococcus Neoformans Meningitis:

- **A.** Amphotericin B at 0.7 mg/kg per day for 7 to 14 days or until clinically stable (maximum total dosage of 2 g), followed by fluconazole 400 mg qd to complete 10 weeks of therapy.
- **B. Suppressive Treatment for Cryptococcus:** Fluconazole (Diflucan) 200 mg PO qd indefinitely.

X. Active Tuberculosis

- **A.** Isoniazid (INH) 300 mg PO qd; and rifampin 600 mg PO qd; and pyrazinamide 15-25 mg/kg PO qd; and ethambutol 15-25 mg/kg PO qd.
- **B.** All four drugs are continued for 2 months; isoniazid and rifampin (depending on susceptibility testing) are continued for a period of at least 9 months and at least 6 months after the last negative cultures.

XI. Disseminated Mycobacterium Avium Complex (MAC):

- **A.** Clarithromycin (Biaxin) 500 mg PO bid; or Azithromycin (Zithromax) 500-1000 mg PO qd **AND**
- **B.** Ethambutol 15-25 mg/kg PO qd (400 mg bid-tid) **AND**
- **C.** Rifabutin 300 mg/d (two 150 mg tablets qd).
- **D. Prophylaxis for MAC:** Rifabutin (Mycobutin), 300 mg PO qd or 150 mg PO bid.

XII. Disseminated Coccidioidomycosis

- **A.** Amphotericin B 0.8 mg/kg IV qd **OR**
- **B.** Fluconazole (Diflucan) 400-800 mg PO and/or IV qd.

XIII. Disseminated Histoplasmosis

- **A.** Amphotericin B 0.5-0.8 mg/kg IV qd, until total dose 15 mg/kg. **OR**
- **B.** Itraconazole (Sporanox) 200 mg PO bid.
- **C. Suppressive Treatment for Histoplasmosis:** Itraconazole (Sporanox) 200 mg PO bid.

Sepsis

I. Pathophysiology

A. Gram-negative organisms are responsible for 50-80% of all cases of septic shock, while 6-24% of cases result from gram-positive organisms. Parasitic infections, disseminated tuberculosis, and systemic fungal disease are less common causes of sepsis.

B. The most common source of gram-negative infection is the genitourinary system.

C. Systemic Inflammatory Response Syndromes (SIRS) is defined as Two or more of the following:

1. Temperature >38° C or <36° C

2. Heart rate >90 beats/min

3. Respiratory rate >20 breaths/min

4. White blood cell count >12,000 or <4,000 or >10% bands

D. SIRS is commonly caused by infection, but a number of other conditions can cause this syndrome (ie, trauma, burns, pancreatitis).

E. Sepsis consists of SIRS plus a documented infection.

F. Severe Sepsis consists of sepsis plus end-organ dysfunction (eg, hypoxemia, elevated lactate, oliguria, altered mentation).

G. Septic Shock is defined as sepsis with hypotension despite fluid resuscitation plus hypoperfusion abnormalities.

H. Refractory Shock is defined as septic shock that lasts more than 1 hour and does not respond to fluid or pressors.

II. Clinical and Laboratory Manifestations of Sepsis

A. The earliest signs of sepsis are tachypnea, respiratory alkalosis, and a moderate hyperdynamic state (increased cardiac output and diminished systemic vascular resistance [SVR]) with little change in blood pressure.

B. As septic shock progresses, hypotension results from a decrease in SVR which may overwhelm the increase in cardiac output. Hypoperfusion is manifested by oliguria, hypoxemia, and lactic acidosis.

C. Fever is common, although. 15% of patients may be hypothermic at onset of bacteremia, and 5% never have a temperature above 99.6° F.

D. Hematologic Abnormalities

1. Disseminated intravascular coagulopathy (DIC) occurs in 10% of septic patients, but only 2-3% have significant bleeding.

2. This syndrome can appear as hemorrhage, thrombosis, or microangiopathic hemolysis.

3. Laboratory findings include decreased platelets and fibrinogen with elevated prothrombin time, partial thromboplastin time, and fibrin degradation products.

4. Neutrophilic leukocytosis with many band forms (left shift) is the most common hematologic change seen in sepsis. Neutropenia is much less common.

E. Renal Effects

1. The effect of sepsis on renal function ranges from minimal proteinuria to acute tubular necrosis, renal failure, and death.

2. Diminished effective circulating volume and hypotension cause renal hypoperfusion with ischemia resulting in acute tubular necrosis.

F. Adult Respiratory Distress Syndrome

1. Sepsis is the most frequent predisposing factor of ARDS. It is

characterized by increased pulmonary capillary permeability resulting in increased extravascular lung water, a widening of the alveolar-arterial 02 gradient, and hypoxemia (PO_2 <65 mm Hg), despite efforts at increased oxygenation (40-50% O_2 by mask).

G. Cutaneous Manifestations

1. **Ecthyma gangrenosum** is the most notable finding, but vesicles, bullae, petechiae, diffuse erythema can occur.
2. Skin lesions should be aspirated, cultured and gram-stained.

III. Clinical Evaluation of Sepsis

A. Blood Cultures: Two to three sets of blood cultures from separate sites are adequate to detect most cases of bacteremia.

B. Gram Strain of Buffy Coat is positive in up to 50% of cases.

C. Hyperglycemia often occurs and may require insulin.

D. Hyperbilirubinemia, minimal transaminase, and alkaline phosphatase elevations are often present because of intrahepatic cholestasis.

Laboratory Tests for Serious Infections

Complete blood count, including leukocyte differential and platelet count Electrolytes Arterial blood gases Blood urea nitrogen and creatinine Urinalysis INR, partial thromboplastin time, fibrinogen Serum lactate	Cultures with antibiotic sensitivities Blood Urine Endometrium (if endometritis suspected) Amniotic fluid (if chorioamnionitis suspected) Wound Other sites (eg, sputum, drains) Chest X-ray Adjunctive imaging studies (eg, computed tomography, magnetic resonance imaging, abdominal X-ray)

IV. Clinical Management of Sepsis

A. Resuscitation

1. Fluid resuscitation can begin with immediate rapid infusion of crystalloid (1-2 L of lactated Ringer's or normal saline over 15-20 minutes). Further hemodynamic therapy should be guided by pulmonary artery catheter pressures.
2. After the initial fluid bolus, crystalloid solution may be administered at 10 mL/min for 15 minutes. If the PCWP does not increase by 3 mm Hg, the 1 liter fluid bolus is repeated. Optimal PCWP is in the range of 10-15 mm Hg.
3. Significant hemodilution may result from the large volumes of fluids; a hemoglobin level of at least 10 g/dL should be maintained.

B. Oxygenation and Ventilation

1. The increased work of breathing and respiratory muscle fatigue during sepsis often necessitates ventilatory support.
2. In the patient with sepsis, oxygen therapy should be started if there is arterial hypoxemia: Oxygen saturation less than 90-92%, or pAO_2 less than 60 mm Hg.
3. Positive end-expiratory pressure is frequently necessary to maintain oxygenation.

C. Vasoactive Drugs

1. Vasoactive drugs are frequently required because of myocardial depression and persistent hypotension.
2. **Dopamine** is the initial drug of choice for improving cardiac function and blood pressure in septic shock. At low doses (1-3 mcg/kg/min), dopamine reacts with dopaminergic receptors, causing vasodilation and increased blood flow in the renal vasculature. At intermediate doses (5-10 mcg/kg/min), beta-adrenergic effects are predominant, which increase myocardial contractility. At high doses (10-20 mcg/kg/min), alpha-adrenergic vasoconstriction is seen including the renal arteries.
3. If dopamine does not adequately support blood pressure, differentiate whether there is persistent vasodilation (blood pressure less than 80 mm Hg with SVR less than 1,400 dynes/s/cm^3) or depressed left ventricular function (low left ventricular stroke work index). If depressed myocardium is the major cause, inotropic therapy with dobutamine should be started; if persistent vasodilation is the problem, a peripheral vasoconstrictor (norepinephrine) should be used.

Commonly Used Vasoactive and Inotropic Drugs

Agent	Dosage
Dopamine	**Renal Perfusion Dose:** 1-3 mcg/kg/min (dopaminergic range) **Cardiac Inotropic Dose:** 5-10 mcg/kg/min (beta-adrenergic) **Vasoconstricting Dose:** 10-20 mcg/kg/min (alpha-adrenergic)
Dobutamine	**Inotropic:** 5-10 mcg/kg/min **Vasodilator:** 15-20 mcg/kg/min
Norepinephrine	2-8 mcg/min
Phenylephrine	20-200 mcg/min
Epinephrine	1-8 mcg/min

D. Treatment of Infection

1. The choice of drugs should be based on the probable source of infection, gram-stained smears of clinical specimens, the immune status of the patient, and local patterns of bacterial resistance.
2. Aggressive dosing of antibiotics is recommended.
3. **Sepsis:** For initial treatment of life-threatening sepsis in adults, a third-generation cephalosporin (cefotaxime, ceftizoxime), ticarcillin/clavulanic acid or imipenem, each together with an aminoglycoside (gentamicin, tobramycin, or amikacin) is recommended.
4. **Methicillin-Resistant Staphylococci:** When MRSA is suspected, treatment with vancomycin (with gentamicin) is recommended.
5. **Intra-Abdominal or Pelvic Infections** are likely to involve anaerobes; treatment should include either ticarcillin/clavulanic acid, ampicillin/sulbactam, piperacillin/tazobactam, imipenem, cefoxitin or cefotetan, each with an aminoglycoside or, alternatively,

metronidazole or clindamycin, together with an aminoglycoside and ampicillin is necessary.

6. **Biliary Tract Infections:** When the source of bacteremia is thought to be in the **biliary tract**, cefoperazone, piperacillin plus metronidazole, piperacillin/tazobactam, or ampicillin/sulbactam, each with an aminoglycoside, should be used.
7. **Antibiotic-Resistant Gram-Negative Bacilli**: In some hospitals, gram-negative bacilli have become resistant to aminoglycosides, third-generation cephalosporins and aztreonam; these strains may be susceptible to imipenem or ciprofloxacin.
8. **Multiple-Antibiotic-Resistant Enterococci**
   a. Many enterococcal strains are now resistant to ampicillin, gentamicin, and vancomycin. A few vancomycin-resistant enterococci are susceptible to teicoplanin (Targocid). Some strains are susceptible to chloramphenicol, doxycycline, or fluoroquinolones.
   b. Quinupristin/dalfopristin (Synercid) (investigational) is active against most strains of multiple-drug-resistant Enterococcus.
   c. Polymicrobial surgical infections that include antibiotic-resistant enterococci may respond to antibiotics aimed at the other organisms.
9. **Dosagees of Antibiotics Used in Sepsis**
   a. Cefotaxime (Claforan) 2 gm q4-6h.
   b. Ceftizoxime (Cefizox) 2 gm IV q8h.
   c. Cefoxitin (Mefoxin) 2 gms q6-8h.
   d. Cefotetan (Cefotan) 2 gms IV q12h.
   e. Ceftazidime (Fortaz) 2 g IV q8h.
   f. Ticarcillin/clavulanate (Timentin) 3.1 gm IV q4-6h (200-300 mg/kg/d).
   g. Ampicillin/Sulbactam (Unasyn) 3.0 gm IV q6h.
   h. Piperacillin/tazobactam (Zosyn) 3.375-4.5 gm IV q6h.
   i. Piperacillin, ticarcillin, mezlocillin 3 gms IV q4-6h.
   j. Imipenem/cilastatin (Primaxin) 0.5-1.0 gm IV q6h (with gentamicin/tobramycin).
   k. Gentamicin, tobramycin 5 mg/kg IV qd; or 100-120 mg (1.5-2 mg/kg) IV, then 80 mg IV q8h (3-5 mg/kg/d).
   l. Amikacin (Amikin) 7.5 mg/kg IV loading dose; then 5 mg/kg IV q8h.
   m. Vancomycin 1 gm IV q12h.
   n. Ofloxacin (Floxin) 400 mg IV q12h.
   o. Aztreonam (Azactam) 1-2 gm IV q6-8h; max 8 g/day.
   p. Metronidazole (Flagyl) 500 mg IV q6-8h.
   q. Clindamycin 600-900 IV q8h (15-30 mg/kg/d).

E. The third-generation cephalosporins (ceftazidime, ceftizoxime, cefotaxime), imipenem or aztreonam can be used to treat sepsis caused by many strains of gram-negative bacilli.

F. Ceftazidime has less activity against gram-positive cocci. Cephalosporins other than ceftazidime and cefoperazone have limited activity against Pseudomonas aeruginosa.

G. Imipenem and aztreonam are active against most strains of P. aeruginosa, and imipenem is active against anaerobes.

H. Aztreonam is active against aerobic gram-negative bacilli, but has poor

activity against gram-positive bacteria and anaerobes.

Peritonitis

Labs: CBC with differential, SMA 12, albumin, LDH, amylase, lactate. PT/PTT, urine, C&S.
Paracentesis
Tube 1 - Cell count and differential (1-2 mL, EDTA purple top tube)
Tube 2 - Gram stain of sediment; C&S, AFB, fungal C&S (3-4 mL); inject 10-20 mL into anaerobic and aerobic culture bottle.
Tube 3 - Glucose, protein, albumin, LDH, triglyceride, specific gravity, amylase, (2-3 mL, red top tube).
Syringe - pH (3 mL).
Note:. Serum/fluid albumin gradient should be determined.
Other Tests: Plain film of abdomen.
CXR PA & LAT, abdominal ultrasound.
Spontaneous Bacterial Peritonitis (nephrotic or cirrhotic):
Option 1:
-Ampicillin* 2 gms IV q 4-6h; **AND EITHER**
Cefotaxime (Claforan) 2 gm IV q4-6h **OR**
Ceftizoxime (Cefizox) 2 gms IV q8h **OR**
Gentamicin or Tobramycin 1.5 mg/kg IV, then 1 mg/kg q8h (adjust for renal function).
Option 2:
-Ticarcillin/clavulanate (Timentin) 3.1 gms IV q6h **OR**
-Piperacillin/tazobactam (Zosyn) 3.375-4.5 gm IV q6h
Option 3:
-Imipenem/cilastatin (Primaxin) 0.5-1.0 gm IV q6h.
*Vancomycin 1 gm IV q12h if penicillin allergic.
Secondary Bacterial Peritonitis:
Option 1:
-Cefotetan (Cefotan) 1-2 gm IV q12h **OR**
-Cefoxitin (Mefoxin) 1-2 gm IV q6h **OR**
-Ampicillin 2 gm IV q4-6h **AND**
Gentamicin or tobramycin (aminoglycosides are not recommended in cirrhotics) 100-120 mg (1.5 mg/kg); then 80 mg IV q8h (5 mg/kg/d) **AND**
Metronidazole 500 mg IV q6-8h
Option 2:
-Piperacillin/tazobactam (Zosyn) 3.375-4.5 gm IV q6h with an aminoglycoside as above **OR**
-Ticarcillin/clavulanate (Timentin) 3.1 gm IV q4-6h (200-300 mg/kg/d) with aminoglycoside as above.
Option 3:
-Ampicillin/Sulbactam (Unasyn) 1.5-3.0 gm IV q6h with aminoglycoside as above.

Option 4:

-Imipenem/cilastatin (Primaxin)1.0 gm IV q6h.

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Gastroenterology

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Hematemesis and Upper Gastrointestinal Bleeding

I. Clinical Evaluation

- **A.** Determine the duration of hematemesis (vomiting bright red blood or coffee ground material), volume of blood, recent hematocrit. Determine whether the bleeding occurred after forceful vomiting (Mallory-Weiss Syndrome).
- **B.** Abdominal pain, melena, hematochezia (bright red blood per rectum); history of peptic ulcer, esophagitis, prior bleeding episodes may be present.
- **C. Precipitating Factors:** Use alcohol, aspirin, nonsteroidal anti-inflammatory agents, steroids, anticoagulants should be sought.
- **D. Past Testing or Treatment:** X-ray studies, endoscopy.
- **E.** The patient may have a past history of gastrointestinal bleeding; prior operations, cardiovascular disease, bleeding disorders.

II. Physical Exam

- **A. General:** Pallor, shallow rapid respirations; tachycardia indicates a 10% blood volume loss; postural hypotension with an increase pulse of 20 and a decrease in systolic of 20 indicates a 20-30% loss.
- **B. Skin:** Delayed capillary refill, pallor. Stigmata of liver disease: Jaundice, spider angiomas, parotid gland hypertrophy.
- **C. Chest:** Gynecomastia (cirrhosis).
- **D. Abdomen:** Scars, tenderness, masses, hepatomegaly; dilated abdominal veins. Stool gross or occult blood.
- **E.** Depressed mental status.

III. Laboratory Evaluation

- **A.** CBC, SMA 12, liver function tests, amylase, PT/PTT, type and cross PRBC, FFP. CBC q6h.
- **B.** EKG, UA. CXR, upright abdomen (evaluate for free air under the diaphragm).

IV. Differential Diagnosis of Upper Bleeding: Peptic ulcer, gastritis, esophageal varices, Mallory Weiss tear (gastroesophageal junction tear because of vomiting or retching), esophagitis, swallowed blood from epistaxis, malignancy (esophageal, gastric), angiodysplasias, aorto-enteric fistula, hematobilia.

V. Diagnostic and Therapeutic Approach to Upper Gastrointestinal Bleeding

- **A.** If the bleeding appears to have stopped or has significantly slowed, medical therapy with H2 blockers, and saline lavage is usually all that is required. The diagnostic and therapeutic approach is based on an estimate of the volume and duration of blood loss, and on the patient's clinical history.
- **B.** Place a minimum of two 14-16 gauge IV lines. Administer 1-2 liters of

normal saline solution until blood is ready, then transfuse PRBC's as fast as possible; estimate blood transfusion requirement based on blood loss rate, vital signs (typically 2-6 units PRBC's are needed). Administer type O negative blood in emergent situations. If hypotensive consider endotracheal intubation.

C. For each 3 units of PRBC transfused, calcium chloride (1 gm IV over an hour) is given to prevent transfusion hypocalcemia.

D. Rapidly assess the patient's need for surgical intervention. Central venous monitoring or pulmonary artery catheter monitoring is necessary in the presence of hypotension or hypoxemia.

E. Place a large bore nasogastric tube, then lavage with 2 L of room temperature tap water, then connect to low intermittent suction, repeat lavage q1h.

F. Administer oxygen by nasal cannula, guided by pulse oximetry. Foley to closed drainage. Keep patient NPO.

G. Record volume and character of lavage. The NG tube may be removed when bleeding is no longer active.

H. If bright red blood is present in nasogastric tube aspirate, lavage with room temperature saline to remove blood clots.

I. Check serial hematocrits, and maintain greater than 30 vol%. Monitor for coagulopathy and correct if necessary with fresh frozen plasma. Consider pulmonary artery catheterization (Swan-Ganz) to assess effectiveness of resuscitation.

J. Definitive diagnosis requires upper endoscopy at which time electrocoagulation of bleeding sites may be completed.

VI. Mallory-Weiss Syndrome

A. This disorder is characterized by a mucosa tear at the gastroesophageal junction. It frequently follows violent retching and vomiting.

B. Treatment is supportive, and the majority of patients stop bleeding spontaneously. Endoscopic coagulation or operative suturing may rarely be necessary.

VII. Medical Treatment of Peptic Ulcers or Nonulcer dyspepsia

A. Ranitidine (Zantac) 50 mg IV bolus, then continuous infusion at 6.25-12.5 mg/h [150-300 mg in 250 mL D5W over 24h (11 cc/h)], or 50 mg IV q6-8h **OR**

B. Cimetidine (Tagamet) 300 mg IV bolus, then continuous infusion at 37.5-50 mg/h (900 mg in 250 mL D5W over 24h), or 300 mg IV q6-8h **OR**

C. Famotidine (Pepcid) 20 mg IV q12h.

Variceal Bleeding

Hemorrhage from esophageal and gastric varices is a severe complication of chronic liver disease.

I. Clinical Evaluation

A. Variceal bleeding should be considered in any patient who presents with significant upper gastrointestinal bleeding, because some patients with liver disease do not exhibit the classic signs of cirrhosis (eg, spider angiomas, palmar erythema, leukonychia, clubbing, parotid enlargement, Dupuytren's contracture).

B. When patients present with jaundice, lower extremity edema and ascites, the diagnosis of decompensated liver disease is obvious.

C. The severity of the bleeding episode can be assessed on the basis of the presence of orthostatic changes (eg, resting tachycardia, postural hypotension), which indicates that about one third or more of blood volume has been lost.

D. If the patient's sensorium is altered because of hepatic encephalopathy, the risk of aspiration mandates endotracheal intubation.

E. Placement of a large-caliber nasogastric tube (22 F or 24 F) permits lavage for removal of blood and clots in preparation for endoscopy.

F. Lavage should be performed with tap water, because saline may contribute to retention of sodium and water.

II. Resuscitation

A. Blood should be replaced as soon as possible. While blood for transfusion is being made available, intravascular volume should be replenished with intravenous albumin in isotonic saline solution (Albuminar-5) or normal saline solution if the patient does not have ascites or evidence of decompensation.

B. Once euvolemia is established, intravenous infusion should be changed to solutions with a lower sodium content (5% dextrose with 1/2 or 1/4 normal saline).

C. Fresh frozen plasma is needed only if massive transfusion is required because of the "washout" phenomenon; in such cases, calcium should also be replaced.

D. Blood should be transfused to maintain a hematocrit of at least 25%. Serial hematocrit estimations during continued bleeding are done to determine whether replacement is adequate. Values may, however, be inaccurate after acute blood loss.

III. Treatment of Variceal Hemorrhage

A. Pharmacologic Agents

1. Octreotide (Sandostatin) 50 mcg IV over 5-10 min, followed by 50 mcg/h for 48 hours (1200 mcg in 250 ml D5W); somatostatin analog; beneficial in controlling hemorrhage.

2. Vasopressin (Pitressin), a posterior pituitary hormone, causes splanchnic arteriolar vasoconstriction and reduction in portal pressure.

a. Dosage is 20 units IV over 20-30 min, then 0.2-0.4 units/minute; complications increase with dosages of 0.4 to 0.6 U/min (100 U in 250 mL D5W).

b. Concomitant use of transdermal nitroglycerin, 0.4 mg/hr for 12 hours may reduce portal pressure by about 10%. This agent mitigates the vasoconstrictor effects of vasopressin on the myocardial and splanchnic circulations.

B. Additional treatments should be considered if bleeding continues, as indicated by fresh blood aspirate from the nasogastric tube and the need for continued blood transfusion (2-3 U of packed cells every 8 hours after start of infusion).

C. Tamponade Devices

1. Bleeding from varices can be reduced with the use of tamponade balloon tubes. However, the benefit is temporary, and prolonged tamponade causes severe esophageal ulceration.

2. The Linton-Nachlas tube is recommended; it has a gastric balloon

and several ports in the esophageal component. The tube is kept in place for 6 to 12 hours while preparations for endoscopic or radiologic treatment are being made.

D. Endoscopic Management of Bleeding Varices

1. Endoscopic sclerotherapy involves injection of a sclerosant solution into varices during endoscopy. The success of the treatment is enhanced by repeating treatments at weekly intervals or less often.
2. **Endoscopic variceal ligation** involves placement of tiny rubber bands on varices during endoscopy.
   - **a.** There are fewer complications with ligation than with sclerotherapy, and bleeding and mortality rates are lower.
   - **b.** Ligation is the preferred treatment when varices are large and there is no active bleeding.

E. Transjugular Intrahepatic Portacaval Shunt (TIPS)

1. Under fluoroscopy, a needle is advanced into the liver through the internal jugular and hepatic veins, and inserted into a large branch of the portal vein. A balloon is then used to enlarge the track to permit the placement of a stent.
2. Because TIPS is a shunt procedure, encephalopathy occurs in about 35% of patients and occlusion of the stent may cause recurrent variceal bleeding.

F. Surgery

1. Portal-systemic shunt surgery is the last resort and the most definitive therapy for bleeding varices. The placement of a shunt creates an anastomosis between portal and systemic veins, allowing decompression of the hypertensive portal venous system and almost complete elimination of rebleeding. However, the procedure has a 30-40% rate of hepatic encephalopathy, and there is no difference in survival rates between shunt surgery and medical treatments.
2. The distal splenorenal shunt is preferred. This shunt is placed between the distal splenic vein and the left renal vein.
3. Portacaval shunt surgery is easier to perform and may be preferable in an emergency or with severe decompensation.

IV. Approach to Treatment of Variceal Hemorrhage

A. Patients initially should be given octreotide (Sandostatin) or vasopressin infusion and transdermal nitroglycerin while awaiting endoscopic treatment.

B. If bleeding is not brisk and varices are large, endoscopic ligation is preferred; for active bleeding from a spurting varix, sclerotherapy is best.

C. Treatment failure warrants the use of TIPS or portal-systemic shunt.

D. Liver transplantation should be considered when other therapy fails.

Lower Gastrointestinal Bleeding

The spontaneous remission rate for lower gastrointestinal bleeding, even with massive bleeding, is 80% (the same as for upper gastrointestinal bleeding). No source of bleeding can be identified in 12%, and bleeding is recurrent in 25%.

Bleeding has usually ceased by the time the patient presents to the emergency room, although copious amounts of blood and clots may continue to be passed from the rectum.

I. Initial Clinical Evaluation

- **A.** The severity of blood loss and hemodynamic status should be assessed immediately. Initial management consists of resuscitation with colloidal solutions (hetastarch [Hespan]) or crystalloid solutions (sodium chloride) and with blood products if necessary.
- **B.** An initial diagnostic evaluation, to determine the source of bleeding, is performed while the patient is being resuscitated.
- **C.** The duration and quantity of bleeding are assessed; however, the duration of bleeding is often underestimated and the quantity is often overestimated.
- **D.** Risk factors that may have contributed to the bleeding should be assessed, such as the use of nonsteroidal anti-inflammatory drugs, anticoagulants, history of colonic diverticulosis, renal failure, coagulopathy, colonic polyps, hemorrhoids, chemotherapy or radiotherapy.
- **E. Hematochezia.** Bright red or maroon blood per rectum suggests a lower GI source; however, 11-20% of patients with an upper GI bleed will have hematochezia as a result of rapid blood loss (these patients are usually in shock).
- **F. Melena.** Sticky, black, foul-smelling stools suggest a source proximal to the ligament of Treitz, but can result from bleeding in the small intestine or proximal colon. Iron and bismuth can turn stools black but not melanotic (shiny and tarry).
- **G. Malignancy** may be indicated by a change in stool caliber, anorexia, weight loss and malaise.
- **H.** Patients may have a history of hemorrhoids, diverticulosis, inflammatory bowel disease, peptic ulcer, gastritis, cirrhosis or esophageal varices.
- **I. Associated Findings**
  1. **Abdominal pain** may result from ischemic bowel, inflammatory bowel disease, or a ruptured aortic aneurysm.
  2. **Painless, massive bleeding** often indicates vascular bleeding from diverticuli, angiodysplasia or hemorrhoids.
  3. **Bloody diarrhea** suggests inflammatory bowel disease or an infectious origin.
  4. **Bleeding with rectal pain** is seen with anal fissures, hemorrhoids, and rectal ulcers.
  5. **Chronic constipation** suggests hemorrhoidal bleeding; new onset constipation or thin stools suggests a left-sided colonic malignancy.
  6. **Blood on the toilet paper or dripping** into the toilet water after a bowel movement indicates a perianal source.
  7. **Blood coating the outside of stool** suggests a lesion in the anal canal.

8. **Blood streaking or mixed in with the stool** may result from a polyp or malignancy in the descending colon.
9. **Maroon colored stools** often indicate small bowel and proximal colon bleeding.

II. Physical Examination

A. Postural Hypotension suggests a 20% blood volume loss; whereas, signs of shock, pallor, hypotension, and tachycardia indicate a 30-40% blood loss.

B. The skin may be cool and pale with delayed capillary refill if bleeding has been significant.

C. Stigmata of liver disease including jaundice, caput medusae, gynecomastia, and palmar erythema should be sought since these patients frequently have GI bleeding.

D. Cutaneous manifestations of the Rendu-Osler-Weber syndrome (telangiectasias) or blue rubber bleb nevus syndrome (blue nevi) should be sought.

III. Approach to the Diagnosis of Lower Gastrointestinal Bleeding

A. Rapid clinical evaluation and resuscitation should precede diagnostic or therapeutic studies. Intravenous fluids (1-2 liters) should be infused over 10-20 minutes to restore intravascular volume, and blood is transfused if there is rapid ongoing blood loss or if hypotension or tachycardia is present. Coagulopathy is corrected with fresh frozen plasma or platelets.

B. When small amounts of bright red blood are passed per rectum, the lower gastrointestinal tract can be assumed to be the source.

C. In patients with large-volume maroon stools, nasogastric tube aspiration should be performed to exclude massive upper gastrointestinal hemorrhage. Occult blood testing of lavage fluid is useless because mild trauma from tube placement may cause a positive result.

D. If the nasogastric aspirate contains no blood, then anoscopy and sigmoidoscopy should be performed to determine whether a colonic mucosal abnormality (ischemic or infectious colitis) or hemorrhoids might be the cause of bleeding.

E. If these measures fail to yield a diagnosis, rapid administration of polyethylene glycol-electrolyte solution (CoLyte) should be initiated orally or by means of a nasogastric tube; 4 L of the lavage solution is infused over a 2- to 3-hour period. This allows diagnostic and therapeutic colonoscopy and adequately prepares the bowel should emergency surgery become necessary.

IV. Causes of Lower Gastrointestinal Bleeding

A. Angiodysplasia and diverticular disease of the right colon account for the vast majority of episodes of acute lower gastrointestinal bleeding.

B. Most acute LGI bleeding originates from the colon; however, 15-20% of episodes arise from the small intestine and the upper gastrointestinal tract.

C. Elderly Patients. Diverticulosis and angiodysplasia are the most common causes of lower GI bleeding.

D. Younger Patients. Hemorrhoids, anal fissures, and inflammatory bowel disease (IBD) are more common causes.

E. Angiodysplasia

1. Angiodysplastic lesions are small vascular tufts that are formed by capillaries, veins, and venules.
2. Angiodysplastic lesions are commonly noted during colonoscopy, appearing as red dots or spider-like lesions 2 to 10 mm in diameter.
3. Angiodysplastic lesions develop secondary, to chronic colonic distention, which leads to obstruction of venules.
4. Angiodysplastic lesions are associated with advanced age, and they have a prevalence rate of 25% in elderly patients These lesions have also been associated with chronic renal failure, CREST syndrome, Rendu-Osler-Weber syndrome, and cirrhosis. Their association with aortic stenosis remains to be established.
5. Even though angiodysplasia may be present throughout the entire colon, the most common site of bleeding remains the right colon. Most patients with angiodysplasia have recurrent minor bleeding; however, massive bleeding is not uncommon.

F. Diverticular Disease

1. Diverticular disease is the most common cause of acute lower gastrointestinal bleeding.
2. 60% to 80% of bleeding diverticula are located in the right colon.
3. 90% of all diverticula are found in the left colon.
4. Diverticular bleeding tends to be massive, but it stops spontaneously in 80% of patients with only supportive care, and the rate of rebleeding is only 25%.

V. Definitive Management of Lower GI Bleeding

A. Colonoscopy

1. Colonoscopy is the procedure of choice for diagnosing colonic causes of gastrointestinal bleeding. It should be performed after adequate preparation of the bowel, which permits identification of 80% of all causative colonic lesions. If the bowel cannot be adequately prepared because of persistent, acute bleeding, a bleeding scan or angiography is preferable.
2. Endoscopy may be therapeutic for angiodysplastic lesions, polyps, and tumors, which can be effectively coagulated.
3. If colonoscopy fails to reveal a source for the bleeding, the patient should be observed, since in about 80% of cases, bleeding ceases spontaneously.

B. Bleeding Scan

1. The technetium-labeled ("tagged") red blood cell bleeding scan can detect bleeding sites when bleeding is intermittent.
2. If the result is positive, the next step is colonoscopy or angiography.

C. Angiography

1. Selective mesenteric angiography detects arterial bleeding that occurs at a rate of 0.5 mL/min or faster.
2. Diverticular bleeding classically causes pooling of contrast medium within a specific diverticulum (extravasation).
3. Bleeding angiodysplastic lesions demonstrate abnormal vasculature.

4. Bleeding from angiodysplastic lesions usually is slow and rarely necessitates therapeutic intervention. However, when active bleeding is seen with diverticular disease or angiodysplasia, selective arterial infusion of vasopressin is effective in arresting hemorrhage in 90%.

D. Evaluation of the Small Bowel

1. If bleeding persists but no source is noted, the small bowel must be considered as a possible source.
2. The preferred technique for evaluating the small bowel is push enteroscopy (with an overtube) in combination with enteroclysis barium study.
3. Meckel's diverticulum, which usually presents in younger patients, is a common site of bleeding in the small intestine. The diagnosis can be confirmed by radionuclide Meckel's scanning, which identifies the ectopic gastric mucosa.

E. Surgery

1. If bleeding continues and no source has been found, surgical intervention is warranted.
2. Surgical resection may be indicated for patients with recurrent diverticular bleeding, or for patients who have had persistent bleeding from colonic angiodysplasia and have required blood transfusions.
3. Treatment of lower gastrointestinal bleeding involves resection of the involved segment--for example, a right hemicolectomy or sigmoid resection. Patients with a diffuse process, such as ulcerative colitis, require a total proctocolectomy with ileostomy.
4. When laparotomy fails to identify a definitive source of bleeding, intraoperative endoscopy may be a useful adjunct.

VI. Colon Polyps and Colon Cancers

A. These rarely cause significant acute LGI hemorrhage.

B. Left-sided and rectal neoplasms are more likely to cause gross bleeding than right sided lesions. Right sided lesions are more likely to cause anemia and occult bleeding.

C. Diagnosis. Colonoscopy.

D. Treatment. Colonoscopic excision or surgery.

VII. Inflammatory Bowel Disease

A. Ulcerative colitis can occasionally cause severe GI bleeding associated with abdominal pain and diarrhea.

B. Diagnosis. Colonoscopy and biopsy.

C. Treatment. Medical treatment of the underlying disease; surgery is required on rare occasions.

VIII. Ischemic Colitis

A. This disorder is seen in elderly patients with known vascular disease; abdominal pain may be postprandial, and is associated with bloody diarrhea or rectal bleeding. Severe blood loss is unusual but can occur.

B. Diagnosis. Abdominal films may reveal "thumbprinting", caused by submucosal edema. Colonoscopy reveals a well-demarcated area of hyperemia, edema, and mucosal ulcerations. The splenic flexure and descending colon are the most common sites.

C. Treatment: Most episodes resolve spontaneously; however, vascular bypass or resection may be required.

IX. Hemorrhoids

A. Hemorrhoids rarely cause massive acute blood loss. In patients with portal hypertension, rectal varices must be sought.

B. Diagnosis. Anoscopy and sigmoidoscopy.

C. Treatment. High fiber diet, stool softeners, or hemorrhoidectomy.

Acute Pancreatitis

I. Diagnosis of Acute Pancreatitis

A. Pancreatitis usually presents as abdominal pain associated with elevated pancreatic enzymes. Pain is typically epigastric or in the left upper quadrant, and the pain is described as constant, dull, or boring; radiation of the pain to the mid-back and worsening in the supine position may occur.

B. Low-grade fever to 101°F is common. Higher temperature may indicate infectious complications. Acute pancreatitis may present with volume depletion, manifesting as hypotension or shock, because of vomiting, hemorrhage, or third spacing of fluid.

C. Patients may have a distended abdomen, and epigastric tenderness and localized rebound may be elicited.

D. Bleeding into the pancreatic bed may rarely manifest as ecchymoses of the flanks (Grey Turner's Sign) or as periumbilical bleeding (Cullen's sign).

II. Etiology: Identification of the etiology of an attack of pancreatitis is essential to prevent recurrences.

A. Alcohol: Alcoholic pancreatitis can develop after an alcohol binge.

B. Gallstones

1. Ultrasonography visualizes gallstones in 75% of patients with "idiopathic" acute pancreatitis.

2. Conditions that Predispose to Biliary Stones: Prolonged fasting (total parenteral nutrition, dieting), pregnancy.

C. Hypertriglyceridemia >1000 mg/dL may cause pancreatitis; lipid-reducing therapy will prevent recurrences.

D. Abdominal Trauma: Trauma such as an automobile accident can result in acute pancreatitis.

E. Postoperative: Pancreatitis may occur after upper abdominal, renal, or cardiovascular surgery.

F. Hypercalcemia: Pancreatitis has been reported with hypercalcemia.

G. Pregnancy: Pancreatitis is most likely during the third trimester and in the 6 weeks postpartum; it is usually related to alcohol or gallstones.

H. Anatomic Causes: Duodenal diverticula, choledochoceles, pancreatic or ampullary strictures, pancreas divisum, or tumors.

I. Infections: Viruses, parasites, and bacteria may cause pancreatitis.

J. Vasculitis: Pancreatitis may be a manifestation of vasculitis.

K. Drugs: Nonsteroidal anti-inflammatory drugs, erythromycin, thiazides, dideoxyinosine (ddI), pentamidine, sulfonamides, and 5-aminosalicylate.

L. Other Causes: Endoscopic retrograde cholangiopancreatography, hereditary pancreatitis, scorpion stings (Trinidad), organophosphate insecticides.

III. Laboratory Evaluation

A. Elevated amylase is not pathognomonic for pancreatitis. Ruptured ectopic pregnancy, tubo-ovarian abscess, ovarian cysts, duodenal perforation, and mesenteric infarction may result in moderate hyperamylasemia. Clearance of amylase is reduced in renal failure, resulting in up to a threefold elevation.

B. In acute pancreatitis the amylase elevation is generally more pronounced than in other settings; values are usually at least 3 times normal. Mild hyperamylasemia may be seen in asymptomatic alcoholics and in acute cholecystitis or cholangitis.

C. An elevated WBC count is common in pancreatitis.

D. Isoamylase Determination: Distinguishes pancreatic amylase from salivary amylase. Elevation of salivary isoamylase occurs with mumps, pneumonia, lung tumors, and breast or prostate cancers.

E. Macroamylasemia

1. An elevation of serum amylase may result from low renal excretion of amylase, and is not an unusual finding in the normal population.

2. Patients with macroamylasemia and pancreatitis may be diagnosed on the basis of an elevated serum lipase.

F. Lipase is more specific for pancreas than amylase.

IV. Imaging Studies

A. Radiographic Studies

1. Flat and upright films of the abdomen help exclude perforated viscus (free air under diaphragm).

2. Nonspecific Findings of Acute Pancreatitis: Adynamic ileus or a sentinel loop (localized jejunal ileus). Pancreatic calcifications may be found with chronic pancreatitis.

B. Ultrasonography

1. Useful for evaluation of the biliary tract for gallstones.

2. Acute pancreatitis is indicated by reduced pancreatic echogenicity, enlargement, or ductal dilation. The pancreas cannot be visualized in 40% because of overlying bowel gas.

C. Computed Tomography (CT) Scanning

1. Contrast-enhanced CT scans have a sensitivity of 90% and a specificity of 100% for the diagnosis of acute pancreatitis.

2. Indications for CT Scan: Acute pancreatitis in patients who are seriously ill or if the diagnosis is uncertain.

D. Endoscopic Retrograde Cholangiopancreatography (ERCP): Not routinely indicated during an attack of acute pancreatitis, but it may be useful in the following situations:

1. Preoperative evaluation of traumatic pancreatitis.

2. Suspected biliary pancreatitis with severe disease that is not improving and may need sphincterotomy and stone extraction.

3. In patients older than 40 years with no identifiable cause, ERCP is indicated once the attack of pancreatitis has subsided to determine the etiology.

V. Assessment of Prognosis

A. Ranson's Criteria

1. Used to assess prognosis early in the course of acute pancreatitis.

2. Overall, mortality from acute pancreatitis is approximately 1% in patients with less than 3 signs, 15% with 3 or 4 signs, 40% with 5 or

6 signs, and 100% with 7 or more signs.

Ranson's Criteria for Alcoholic Pancreatitis

At Admission:	**During Initial 48 Hours:**
1. Age over 55 years 2. WBC >16,000/mm^3 3. Blood glucose >200 mg/dL (in a nondiabetic) 4. Serum LDH >350 IU/L 5. AST >250 U/L	1. Hematocrit drop >10% points 2. BUN rise >5 mg/dL 3. Arterial PO2 <60 mm Hg 4. Base deficit >4 mEq/L 5. Serum calcium <8.0 mg/dL 6. Estimated fluid sequestration >6 L

Ranson's Criteria for Nonalcoholic Pancreatitis

Admission	**Initial 48 hours**
1. Age over 70 years 2. WBC > 18,000/mm^3 3. Blood glucose > 220 mg/dL (in a nondiabetic) 4. Serum LDH > 400 IU/L 5. AST > 250 U/L	1. Hematocrit drop > 10% points 2. BUN rise > 2 mg/dL 3. Base deficit > 5 mEq/L 4. Serum calcium < 8.0 mg/dL 5. Estimated fluid sequestration > 4 L

VI. Complications of Pancreatitis

- **A. Pseudocyst** is a pancreatic fluid collection that may regress, or it may progress to a mature pseudocyst.
- **B. Necrotizing pancreatitis** occurs after infection of the necrotic pancreatic tissue, often within 6 days after the episode begins.
- **C. Shock, adult respiratory distress syndrome** (ARDS), renal failure, and gastrointestinal bleeding are occasional complications.

VII. Medical Management of Pancreatitis

- **A. Supportive Medical Care for Local and Systemic Complications:** The majority of patients (>80%) have rapid resolution of the inflammatory process and a noncomplicated course.
- **B. Replace Intravascular Volume:** Ringer's lactate, normal saline or colloids (albumin) are administer to restore hemodynamic stability and to maintain a urine output of 0.5-1 cc/kg/h. Monitor central venous pressure and replace calcium and magnesium deficits.
- **C. Pancreatic Rest:** Oral feeding is withheld until nausea, vomiting, and abdominal pain have subsided. Total parenteral nutrition is usually necessary. After acute symptoms have resolved, feeding may be started, with gradual progression from liquids to a regular diet.
- **D. Nasogastric Suction** is used if severe nausea, vomiting, or ileus is present.
- **E. Antibiotics:** Prophylactic antibiotics are used with a temperature >101.5°F, cholangitis, or severe pancreatitis. Cefoxitin (Mefoxin) 1-2 gm IV q6h **OR**
  Cefotetan (Cefotan) 1-2 gm IV q12h.
- **F. Analgesics:** Meperidine (Demerol) should be used because morphine may cause spasm of the sphincter of Oddi.
- **G. Medical Management**
  1. Somatostatin 250 mcg IV bolus, followed by 100 mcg/h x 48 hours **OR**
  2. Octreotide (Sandostatin) 100-200 mcg SC three times per day.

3. Ranitidine (Zantac) 50 mg IV q8h **OR**
4. Cimetidine (Tagamet) 300 mg IV q8h.
5. Insulin may be needed if there is severe hyperglycemia.
6. Alcohol withdrawal prophylaxis may be required with chlordiazepoxide 50-100 mg IV/IM q6h round the clock x 3 days, thiamine 100 mg IM/IV qd x 3d; folic acid 1 mg IM/IV qd x 3d; multivitamin qd.

VIII. Surgical Management of Pancreatitis

A. Surgical Management is indicated to exclude other intra-abdominal processes, or if abscess, infection, necrotizing pancreatitis, or pseudocyst.

B. Operative management should be guided by CT imaging.

C. A cholecystectomy is indicated for biliary pancreatitis. The procedure is usually performed early, usually on hospital day 3 or 4 when amylase has returned to normal. Surgery may be performed during the acute attack if deterioration occurs. Endoscopic sphincterotomy is useful to remove obstructing stones.

D. Severe necrotizing pancreatitis requires necrosectomy to remove necrotic pancreatic tissue and septic material. This is followed by local lavage and placement of drains.

IX. Pancreatic Pseudocyst

A. Clinical signs of pseudocyst include continuing abdominal pain, vomiting, nausea, epigastric tenderness, abdominal mass, and hyperamylasemia. CT and ultrasound are diagnostic.

B. Pseudocyst Management

1. Pseudocysts are managed expectantly for 6-8 weeks until a mature cyst wall develops.
2. Pseudocysts that are less than 5 cm in diameter usually resolve spontaneously.
3. After a mature cyst wall has developed, internal drainage by cystogastrostomy, cystojejunostomy, or cystoduodenostomy is completed. A malignant pseudocyst should be excluded by biopsy of cyst wall.
4. Percutaneous, CT guided drainage may be considered after thickening of cyst wall has occurred.

Hepatic Encephalopathy

I. History and Physical: Lethargy, confusion, stupor, and coma. Physical exam may reveal hepatosplenomegaly, ascites, jaundice, spider angiomas, gynecomastia, testicular atrophy, and asterixis.

II. Labs: Ammonia, CBC, platelets, SMA 12, Mg, Cal, SGOT, SGPT, SGGT, LDH, alkaline phosphatase, protein, albumin, bilirubin, PT/PTT, ABG, hepatitis panel. UA. CXR, ECG, urine and blood drug screen. Blood and urine cultures.

III. General Measures: Avoid sedatives, diuretics, NSAIDS or hepatotoxic drugs. Turn patient q2h while awake, chart stools. Foley to closed drainage. Signs of infection should be sought.

IV. Treatment

A. Lactulose 30-45 mL PO q1h x 3 doses, then 15-45 mL PO bid-qid titrate

to produce 2 soft stools/d **OR**

B. Lactulose enema (300 mL of lactulose in 700 mL of tap water) 250 mL PR q6h (clamp rectal tube for 45 min) **OR**

C. Neomycin, 0.5-1.0 gm PO/NG q4-6h, is given if encephalopathy persists despite lactulose; avoid if azotemic **OR**

D. Milk of magnesia 30 mg PO x 1 dose before starting lactulose (avoid if inadequate renal function.)

E. Electrolyte abnormalities and infection are treated.

V. Nutrition and Other Measures

A. Ranitidine (Zantac) 50 mg IV q6-8h or 150 mg PO bid **OR**

B. Cimetidine (Tagamet) 300 mg IV q6-8h or 300 mg PO tid-qid **OR**

C. Famotidine (Pepcid) 20 mg IV/PO q12h

D. Vitamin K 10 mg SQ qd x 3d.

E. Multivitamin PO qAM or 1 ampule IV qAM.

F. Folic acid 1 mg PO/IV/IM qd.

G. Thiamine 100 mg PO/IV/IM qd.

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78 Hepatic Encephalopathy

Toxicology

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Poisoning and Drug Overdose

I. Management of Poisoning and Drug Overdose:

A. Stabilize vital signs; maintain airway, breathing and circulation.

B. Consider intubation if patient has depressed mental status and is at risk for aspiration or respiratory failure.

C. Establish IV access and administer oxygen.

D. Draw blood for baseline labs (see below).

E. If altered mental status is present, administer D50W 50 mLs IV push, followed by naloxone (Narcan) 2 mg IV, followed by thiamine 100 mg IV.

F. If no improvement, evaluate for other causes of altered mental status.

II. Gastrointestinal Decontamination

A. Gastric Lavage

1. **Contraindications:** Acid, alkali, hydrocarbon, or sharp object ingestion.
2. Consider intubation for airway protection if depressed mental status.
3. Place the patient in Trendelenburg's position and left lateral decubitus. Insert a large bore (32-40) french Ewald orogastric tube. A smaller NG tube may be used but may be less effective in retrieving large particles.
4. After tube placement has been confirmed by auscultation, aspirate stomach contents and lavage with 200 cc aliquots of saline or water until clear (up to 2 L).
5. Send the first 100 cc for toxicology analysis.

B. Activated Charcoal (AC)

1. Not effective for alcohols, aliphatic hydrocarbons, caustics, cyanide, elemental metals (boric acid, iron, lithium, lead), or pesticides.
2. Oral or nasogastric dose is 50 gm mixed with sorbitol. Repeat dose of 25-50 gm q4-6h for 24-48 hours if massive ingestion, sustained release products, tricyclic antidepressants, phenothiazines, sertraline, paroxetine, carbamazepine, digoxin, phenobarbital, phenytoin, valproate, salicylate, doxepin, or theophylline were ingested.
3. Give oral cathartic with charcoal (70% sorbitol). Use magnesium with caution in renal insufficiency.

C. Whole Bowel Irrigation (WBI)

1. Can prevent further absorption in cases of massive ingestion, delayed presentation, or in overdoses of enteric coated or sustained release pills.
2. May be useful in eliminating objects, such as batteries, or ingested packets of drugs.
3. Administer GoLytely, or Colyte orally at 1.6 - 2.0 l/hour until fecal effluent is clear. Contraindicated in patients with ileus.

D. Hemodialysis: Indications include ingestion of phenobarbital, theophylline, chloral hydrate, salicylate, ethanol, lithium, ethylene glycol, isopropyl alcohol, procainamide, and methanol, or severe metabolic acidosis.

E. Hemoperfusion (charcoal or resin):
1. May be more effective than hemodialysis **except** for bromides, heavy metals, lithium, and ethylene glycol.
2. Effective for disopyramide, phenytoin, barbiturates, theophylline.

Toxicologic Syndromes

I. Characteristics of Common Toxicologic Syndromes:
- **A. Cholinergic (muscarinic) Poisoning:** Salivation, defecation, lacrimation, emesis, urination, miosis.
- **B. Anticholinergic Poisoning:** Dry skin, flushing, fever, urinary retention, mydriasis, thirst, delirium, conduction delays, tachycardia, ileus.
- **C. Sympathomimetic Poisoning:** Agitation, hypertension, seizure, tachycardia, mydriasis, vasoconstriction.
- **D. Narcotic Poisoning:** Lethargy, hypotension, hypoventilation, miosis, coma, ileus.
- **E. Withdrawal Syndrome:** diarrhea, lacrimation, mydriasis, cramps, tachycardia, hallucination.
- **F. Common Causes of Toxic Seizures:** Amoxapine, anticholinergics, camphor, carbon monoxide, cocaine, ergotamine, isoniazid, lead, lindane, lithium, LSD, parathion, phencyclidine, phenothiazines, propoxyphene HCL, propranolol, strychnine, theophylline, tricyclic antidepressants.
- **G. Common Causes of Toxic Cardiac Arrhythmias:** Arsenic, beta-blockers, chloral hydrate, chloroquine, clonidine, calcium channel blockers, cocaine, cyanide, carbon monoxide, digitalis, ethanol, phenol, phenothiazine, tricyclics.

Acetaminophen Overdose

I. Clinical Features

A. Acute lethal dose = 13 - 25 g. Acetaminophen is partly metabolized to N-acetyl-p-benzoquinonimine which is conjugated by glutathione. Hepatic glutathione stores can be depleted in acetaminophen overdose, leading to centrilobular necrosis.

B. Signs and Symptoms
1. Liver failure occurs 3 days after ingestion if untreated. Liver failure presents with right upper quadrant pain, elevated liver function tests, coagulopathy, hypoglycemia, renal failure and encephalopathy.

II. Treatment

A. Gastrointestinal Decontamination: Gastric lavage followed by activated charcoal. Remove residual charcoal with saline lavage prior to giving N-Acetyl-Cysteine (NAC).

B. Check 4-hour, post ingestion acetaminophen level. Use nomogram to determine if treatment is necessary (see next page). Start treatment if level is above the nontoxic range or if the level is potentially toxic but the time of ingestion is unknown.

C. Therapy must start no later than 8-12 hours after ingestion. Treatment

after 16-24 hours of non-sustained release formulation is significantly less effective, but should still be accomplished.

D. Oral N-Acetyl-Cysteine: 140 mg/kg PO followed by 70 mg/kg PO q4h x 17 doses (total 1330 mg/kg over 72 h). Repeat loading dose if emesis occurs.

E. If oral route is not possible, the following protocol is available (but not FDA approved): NAC 150 mg/kg in 200 mL D5W IV over 15 min, followed by 50 mg/kg in 500 mL D5W IV over 4h, followed by 100 mg/kg in 1000 mL D5W IV over next 16 hours. Filter solution through 0.22 micron filter prior to administration. Complete all PO/NG/IV doses even after acetaminophen level falls below critical value.

F. Hemodialysis and hemoperfusion are somewhat effective, but should not take the place of NAC treatment.

Cocaine Overdose

I. Clinical Evaluation

A. Cocaine can be used intravenously, smoked, ingested, or inhaled nasally. The effect of oral cocaine is equivalent to the intranasal route.

B. Street cocaine comes in unreliable concentrations, and often is cut with other substances including amphetamines, LSD, PCP, heroin, strychnine, lidocaine, talc, and quinine.

C. One-third of fatalities occur within 1 hour, with another third occurring 6 to 24 h later.

D. Be aware of "body packers" who transport cocaine by swallowing well wrapped packets, and "body stuffers" who hastily swallow packets of cocaine to avoid arrest.

II. Clinical Features

A. CNS: Sympathetic stimulation, agitation, seizures, tremor, headache, subarachnoid hemorrhage, ischemic cerebral stoke, psychosis, hallucinations, fever, mydriasis, formication (sensation of insects crawling on skin).

B. Cardiovascular: Atrial and ventricular arrhythmias, myocardial infarction, hypertension, hypotension, myocarditis, aortic rupture, cardiomyopathy.

C. Pulmonary: Noncardiogenic pulmonary edema, pneumomediastinum, alveolar hemorrhage, hypersensitivity pneumonitis, bronchiolitis obliterans.

D. Other: Rhabdomyolysis, mesenteric ischemia, hepatitis.

III. Treatment:

A. Supportive care is administered because no antidote exists.

B. GI Decontamination, including repeated activated charcoal, whole bowel irrigation and endoscopic evaluation is provided if oral or packet ingestion is suspected.

C. Treat hyperadrenergic symptoms with benzodiazepines such as diazepam.

D. Seizures

1. Treat with diazepam, phenytoin, or phenobarbital.

2. Evaluate for other possible causes of seizures such as subarachnoid hemorrhage, hypoxemia, and hypoglycemia.

E. Arrhythmias
1. Treat hyperadrenergic state and supraventricular tachycardia with diazepam and propranolol.
2. Treat ventricular arrhythmias with lidocaine or propranolol may be required.

F. Hypertension
1. Use diazepam first for tachycardia and hypertension.
2. If no response, use labetalol for alpha and beta blocking effects.
3. If hypertension remains severe, consider sodium nitroprusside and esmolol drips.

G. Myocardial Ischemia and Infarction
1. Treat with thrombolysis, heparin, aspirin, beta-blockers.
2. Control hypertension and consider possibility of CNS bleeding before using thrombolytic therapy.

Cyclic Antidepressant Overdose

I. Clinical Features

A. Cyclic antidepressants have a large volume of distribution (15-40 L/kg), high lipid solubility, high protein binding. Antidepressants have prolonged body clearance rates, and can not be removal by forced diuresis, hemodialysis, and hemoperfusion.

B. Delayed absorption is common because of decreased GI motility from anticholinergic effects.

C. Cyclic antidepressants undergo extensive enterohepatic recirculation.

D. CNS: Lethargy, coma, hallucinations, seizures, myoclonic jerks.

E. Anticholinergic crises: Blurred vision, dilated pupils, urinary retention, dry mouth, ileus, hyperthermia.

F. Cardiac: Hypotension, ventricular tachyarrhythmias, heart block.

G. EKG: Sinus tachycardia, right bundle branch block, right axis deviation, increased PR and QT interval, QRS >100 msec, or right axis deviation. Prolongation of the QRS width is a more reliable predictor of CNS and cardiac toxicity than the TCA level.

II. Treatment

A. Gastrointestinal Decontamination and Systemic Drug Removal
1. Magnesium citrate 300 mLs via nasogastric tube x 1 dose.
2. Activated charcoal premixed with sorbitol 50 gms via nasogastric tube q4-6h around-the-clock until TCA level decreases to therapeutic range. Maintain the head-of-bed at a 30-45 degree angle to prevent aspiration.
3. **Cardiac Toxicity**
   - **a.** Alkalinization is a cardioprotective measure and it has no influence on drug elimination. Treatment goal is to achieve an arterial pH of 7.50-7.55.
   - **b.** If mechanical ventilation is necessary, hyperventilate to maintain desired pH.
   - **c.** Administer sodium bicarbonate 50-100 mEq (1-2 amps or 1-2 mEq/kg) IV over 5-10 min. Followed by infusion of sodium bicarbonate, 2 amps in 1 liter of D5W at 100-150 cc/h. Adjust IV rate to maintain desired pH.

4. **Seizures**
   a. Lorazepam or diazepam IV followed by phenytoin.
   b. Physostigmine, 1-2 mg slow IV over 3-4 min, is necessary if seizures continue.

Digoxin Overdose

I. Clinical Features

A. Therapeutic window is 0.8-2.0 ng/mL.

B. Drug-drug interactions that increase digoxin levels include verapamil, quinidine, amiodarone, flecainide, erythromycin, and tetracycline.

C. Hypokalemia, hypomagnesemia and hypercalcemia enhance digoxin toxicity.

D. CNS: Confusion, lethargy; yellow-green visual halo.

E. Cardiac: Any dysrhythmia can be seen including atrial fibrillation and flutter; ventricular tachycardia or fibrillation; variable atrioventricular block, atrioventricular dissociation; sinus bradycardia, junctional tachycardia, premature ventricular contractions.

F. GI: Nausea, vomiting.

G. Metabolic: Hyperkalemia is common but may be normal or low in patients on diuretics.

II. Treatment

A. Gastrointestinal Decontamination: Gastric lavage, followed by repeated doses of activated charcoal is effective; hemodialysis is ineffective.

B. Treat bradycardia with atropine, isoproterenol, and cardiac pacing.

C. Treat ventricular arrhythmias with lidocaine or phenytoin. Avoid procainamide and quinidine as they may be proarrhythmic and slow AV conduction.

D. Electrical DC cardioversion may be dangerous in severe toxicity, and should be used judiciously and at low energy settings.

E. Hypomagnesemia and hypokalemia should be corrected.

F. Digibind (Digoxin - specific Fab antibody fragment):

1. Indication: life threatening arrhythmias refractory to conventional therapy.

2. Dosage of Digoxin immune Fab

$$\text{(number of 40 mg vials)} = \frac{\text{Digoxin level (ng/mL) x body weight (kg)}}{100}$$

3. Dissolve the digoxin immune Fab in 100-150 mLs of NS and infuse IV over 15-30 minutes. Use a 0.22 micron in-line filter during infusion.

4. Hypokalemia, heart failure, and anaphylaxis may occur. The complex is renally excreted; after administration, serum digoxin level may be high and inaccurate because both free and bound digoxin is measured with certain assays.

Ethylene Glycol Ingestion

I. Clinical Features

A. Ethylene glycol is found in antifreeze, detergents, and polishes.

B. Toxicity: Half-life 3-5 hours; the half-life increases to 17 hours if coingested with alcohol; minimal lethal dose 1.0-1.5 cc/kg; lethal blood level 200 mg/dL.

C. Anion gap metabolic acidosis and severe osmolar gap is often present.

D. CNS depression; cranial nerve dysfunction (facial and vestibulocochlear palsies).

E. GI symptoms such as flank pain; oxalate crystals in urine sediment; hypocalcemia (due to calcium oxalate formation); tetany, seizures, and prolonged QT may occur.

II. Treatment

A. Ethanol 10% (in D5W) as 7.5 cc/kg IV load, then 1.4 cc/kg/h IV drip to keep blood alcohol level between 100-150 mg/dL and to keep serum ethylene glycol level <10 mg/dL.

B. Pyridoxine 100 mg IV qid x 2 days and thiamine 100 mg IV qid x 2 days; may increase metabolism of glyoxylate.

C. If definitive therapy is not immediately available, 3-4 ounces of whiskey (or equivalent) may be given orally.

D. Hemodialysis

1. Indications: Severe acidosis, crystalluria, serum ethylene glycol level >50 mg/dL; keep glycol level <10 mg/dL.

Isopropyl Alcohol Ingestion

I. Clinical Features

A. Isopropyl alcohol is found in rubbing alcohol, solvents, and antifreeze.

B. Toxicity: Lethal dose: 3-4 g/kg

1. Lethal blood level: 400 mg/dL

2. Half life = 3 hours

C. Metabolism: Isopropyl alcohol is metabolized to acetone.

D. Toxicity is characterized by an anion gap metabolic acidosis with high serum ketone level; mild osmolar gap; mildly elevated glucose.

E. CNS depression, headache, nystagmus; cardiovascular depression, abdominal pain and vomiting, and pulmonary edema.

II. Treatment

A. Provide supportive care. No antidote is available; ethanol is not indicated.

B. Hemodialysis: Indications: refractory hypotension, coma, potentially lethal blood levels.

Methanol Ingestion

I. Clinical Features

A. Methanol is found in antifreeze, Sterno, cleaners, and paints.

B. Toxicity:

1. 10 cc causes blindness

2. Minimal lethal dose = 1-5 g/kg

3. Lethal blood level = 80 mg/dL

4. Symptomatic in 40 minutes to 72 hours.

C. Signs and Symptoms:

1. Severe osmolar and anion gap metabolic acidosis.

2. Visual changes occur because of optic nerve toxicity, leading to blindness.

3. Nausea, vomiting, abdominal pain, pancreatitis, and altered mental status.

II. Treatment

A. Ethanol 10% is infuse in D5W) as 7.5 cc/kg load then 1.4 cc/kg/h drip to keep blood alcohol level between 100-150 mg/dL. Continue therapy until methanol level is below 20-25 mg/dL.

B. Give folate 50 mg IV q4h to enhance formic acid metabolism.

C. Correct acidosis and electrolyte imbalances.

D. Hemodialysis: Indications: peak methanol level >50 mg/dL; formic acid level >20 mg/dL; severe metabolic acidosis; acute renal failure; any visual compromise.

Iron Overdose

I. Clinical Features

A. Toxicity is caused by free radical organ damage and damage to the GI mucosa, liver, kidney, heart, and lungs. The cause of death is usually shock and liver failure.

Toxic dosages and serum levels

Nontoxic	<10-20 mg/kg (0-100 mcg/dL)
Toxic	>20 mg/kg (350-1000 mcg/dL)
Lethal	>180-300 mg/kg (>1000 mcg/dL)

B. Two Hours After Ingestion: Severe hemorrhagic gastritis; vomiting, diarrhea, lethargy, tachycardia, and hypotension.

C. Twelve Hours After Ingestion: Improvement and stabilization.

D. 12-48 Hours After Ingestion: GI bleeding, coma, seizures, pulmonary edema, circulatory collapse, hepatic and renal failure, coagulopathy, hypoglycemia, and severe metabolic acidosis.

II. Treatment

A. Administer deferoxamine. 100 mg of deferoxamine binds 9 mg of free elemental iron.

B. Deferoxamine Dosage: IM 40-90 mg/kg; max 2 gm per injection or 6 gms per day. IV 15 mg/kg/h; max 6 gms per day.

C. Treat until 24 hours after vin rose colored urine clears. Serum iron levels during chelation are not accurate.

D. Gastrointestinal Decontamination

1. Charcoal is not effective in absorbing elemental iron. Evaluate x-rays for remaining iron tablets. Consider whole bowel lavage if iron pills are past the stomach and cannot be removed by gastric lavage (see page 79).

2. Hemodialysis is considered for severe toxicity.

Lithium Overdose

I. Clinical Features

A. Lithium has a narrow therapeutic window of 0.8-1.2 mEq/l.

B. Drug-drug interactions will increase lithium levels: NSAID's, phenothiazines, and thiazides.

C. Toxicity:
1.5-3.0 mEq/l = moderate toxicity
3.0-4.0 mEq/l = severe toxicity

D. Toxicity in chronic lithium users occurs at much lower serum levels than with acute ingestions.

E. Common manifestations include seizures, encephalopathy, hyperreflexia, tremor, nausea, vomiting, diarrhea, hypotension; nephrogenic diabetes insipidus, hypothyroidism.

F. Conduction block and dysrhythmias are rare, but reversible T wave depression may occur.

II. Treatment

A. Correct hyponatremia.

B. Follow lithium levels until <1.0 mEq/l and watch for rebound as levels may increase from intracellular stores.

C. Forced Solute Diuresis: Hydrate with normal saline infusion to maintain urine output at 2-4 cc/kg/hr; use furosemide (Lasix) 40-80 mg IV doses as needed.

D. GI Decontamination

1. Administer gastric lavage. Activated charcoal is ineffective. Whole bowel irrigation may be useful.

2. Indications for Hemodialysis: Level >4 mEq/l; chronic ingestion with symptoms; CNS or cardiovascular impairment with level of 2.5-4.0 mEq/l.

Salicylate Overdose

I. Clinical Features

A. Toxicity

150-300 mg/kg - mild toxicity
300-500 mg/kg - moderate toxicity
>500 mg/kg - severe toxicity

B. Chronic use can cause toxicity at much lower levels (ie, 25 mg/dL) than occurs with acute use.

C. Acid/Base Abnormalities: Patients present initially with a respiratory alkalosis because of central hyperventilation; later an anion gap metabolic acidosis occurs.

D. CNS: Tinnitus, lethargy, irritability, seizures, coma, cerebral edema.

E. GI: Nausea, vomiting, liver failure, GI bleeding.

F. Cardiac: Hypotension, sinus tachycardia, AV block, wide complex tachycardia.

G. Pulmonary: Non-cardiogenic pulmonary edema, adult respiratory distress syndrome.

H. Metabolic: Renal failure; coagulopathy because of decreased factor VII; hyperthermia because of uncoupled oxidative phosphorylation.

II. Treatment

A. Provide supportive care and GI decontamination. Aspirin may form concretions or drug bezoars, and ingestion of enteric coated preparations may lead to delayed toxicity.

B. Multiple dose activated charcoal, whole bowel irrigation, and serial salicylate levels are indicated.

C. Treat hypotension and dehydration vigorously with fluids, and correct electrolytes, especially potassium. Maintain urine output at 200 cc/h or more.

D. Correct metabolic acidosis with bicarbonate 50-100 mEq (1-2 amps) IVP.

E. Renal clearance is increased by alkalinization of urine with an IV bicarbonate infusion (2-3 amps in 1 liter of D5W at 150-200 mL/h), keeping the urine pH at 7.5-8.5.

F. Hemodialysis or charcoal hemoperfusion

1. Indications: Seizures, cardiac or renal failure, intractable acidosis, acute salicylate level >120 mg/dL or chronic level >50 mg/dL (therapeutic level 15-25 mg/dL).

2. Hemoperfusion is effective in clearance of salicylate, but less effective at correcting electrolyte and acid-base imbalances.

Theophylline Toxicity

I. Clinical Features

A. Drug interactions can increase serum theophylline level, including quinolone and macrolide antibiotics, propranolol, cimetidine, and oral contraceptives.

B. Liver disease or heart failure will decrease clearance.

C. Serum Toxicity levels:
20-40 mg/dL - mild
40-70 mg/dL - moderate
>70 mg/dL - life threatening

D. Toxicity in chronic users occurs at lower serum levels than with short-term users. Seizures and arrhythmias can occur at therapeutic or minimally supra-therapeutic levels.

E. CNS: Hyperventilation, agitation, and tonic-clonic seizures.

F. Cardiac: Sinus tachycardia, multi-focal atrial tachycardia, supraventricular tachycardia, ventricular tachycardia and fibrillation, premature ventricular contractions, hypotension or hypertension.

G. GI: Vomiting, diarrhea, hematemesis.

H. Musculoskeletal: Tremor, myoclonic jerks

I. Metabolic: Decreased potassium, magnesium, phosphate, and increased glucose and calcium.

II. Treatment

A. GI Decontamination and Systemic Drug Removal

1. Activated charcoal premixed with sorbitol, 50 gms PO or via nasogastric tube q4-6h around-the-clock until theophylline level <20 mcg/mL. Maintain head-of-bed at 30 degrees to prevent charcoal aspiration.

2. Indications for Charcoal Hemoperfusion: Coma, seizures, hemodynamic instability, theophylline level >60 mcg/mL; rebound in serum levels may occur after discontinuation of hemoperfusion.

3. Seizures may be refractory to standard therapy with diazepam, dilantin, and phenobarbital.

4. Treat Hypotension with fluids.

a. Norepinephrine 8-12 mcg/min IV infusion or

b. Phenylephrine 0.04-1.8 mg/min IV infusion.

5. Treatment of Arrhythmias

a. Lidocaine 1 mg/kg loading up to 3 mg/kg, then 1-4 mg/min continuous IV drip **OR**

b. Esmolol (Brevibloc) 500 mcg/kg/min loading dose, then 50-300 mcg/kg/min continuous IV drip.

Warfarin (Coumadin) Overdose

I. Clinical Management

A. Elimination Measures: Gastric lavage and activated charcoal if recent oral ingestion of warfarin (Coumadin).

B. Reversal of Coumadin Anticoagulation: Coagulopathy may be corrected rapidly or slowly depending on the following factors: 1)

Intensity of hypocoagulability, 2) severity or risk of bleeding, 3) need for reinstitution of anticoagulation.

C. Emergent Reversal:

1. Fresh frozen plasma: Replace Vitamin K dependent factors with FFP 2-4 units; repeat in 4 hours if prothrombin time remains prolonged.
2. Vitamin K 25 mg in 50 cc NS to infuse no faster than 1 mg/min; risk of anaphylactoid reactions and shock; slow infusion minimizes risk.

D. Reversal over 24-48 Hours: Vitamin K 10-25 mg subcutaneously. Full reversal of anticoagulation will result in resistance to further Coumadin therapy for several days.

E. Partial Correction: Lower doses of Vitamin K (0.5-1.0 mg) will lower prothrombin time without interfering with reinitiation of Coumadin.

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90 Warfarin Overdose

Neurology

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Stroke

I. Clinical Evaluation of the Stroke Patient

A. Determine when symptoms started and stopped, and whether symptoms had an abrupt or gradual onset. Hemorrhages and embolic strokes typically appear suddenly; thrombotic strokes may have a more stuttering course, with progressive neurologic symptoms such as spreading numbness or weakness.

B. A history of transient ischemic attacks (TIA), especially in a crescendo pattern, is a strong predictor of ischemic stroke. About 30% of patients with TIAs go on to have full-blown strokes, although less than half of patients have had a preceding TIA before a ischemic stroke.

C. Markers of vascular disease such as diabetes, angina pectoris, and intermittent claudication indicate cerebral infarction. A history of atrial fibrillation or MI suggests ischemic stroke from a cardiac embolus.

D. Sudden, explosive, headache pain, which is typically describes as "the worst headache of my life," is the classic sign of subarachnoid hemorrhage. Head pain is less common in ischemic strokes. Increased intracranial pressure from intracranial bleeding is also likely to trigger an emetic response or syncope. Other signs of subarachnoid hemorrhage include impaired consciousness, photophobia, and a stiff neck.

E. In younger people, about half of all strokes are hemorrhagic; in older people, 20-25% are hemorrhagic.

F. Migraine can cause pain severe enough to mimic subarachnoid hemorrhage, but migraines appear gradually (often with an aura), rather than suddenly. Hemiplegic migraine is more common in young women, who are unlikely to have atherosclerotic disease.

G. Vertebrobasilar circulation syndromes are characterized by double vision, facial weakness, vertigo, and weakness or numbness on both sides of the body.

H. Cocaine-related strokes are not common but should be considered in young adults; cocaine may be associated with either ischemia or hemorrhage.

II. Neurologic Examination

A. Determine whether the patient's condition is acutely deteriorating or relatively stable.

B. Immediate Assessment: Level of consciousness, orientation; ability to speak and understand language; cranial nerve function, especially eye movements and pupil reflexes, facial paresis; neglect, gaze preference, arm and leg strength, sensation, and walking ability.

C. A semiconscious or unconscious patient probably has a hemorrhage. A patient with an ischemic stroke may be drowsy but is unlikely to lose consciousness unless the infarcted area is large.

D. All patients should be evaluated for the need for immediate surgery if there are signs of intracerebral or subarachnoid hemorrhage. Hydrocephalus after subarachnoid hemorrhage may be delayed, and

may present with lethargy, stupor, gait difficulties, urinary incontinence, and cognitive dysfunction.

E. Left hemispheric syndromes are characterized by right-sided weakness with aphasia.

F. The higher the initial BP, the more likely the stroke is a cerebral hemorrhage.

III. CT Scanning and Diagnostic Studies

A. All patients with signs of stroke should undergo a noncontrast head CT to screen for bleeding and to rule out expanding lesions such as subdural hematomas, epidural hematomas, or other indications for emergent surgery.

B. An initially negative CT scan is common early in ischemic strokes. CT is the most definitive modality for detecting intracranial hemorrhages, but in infarction, it does not detect the full extent of tissue damage until several days later. If the screening CT scan is equivocal or negative, consider MRI to localize a cerebral infarct; gadopentetate (Magnevist) contrast media may be used.

C. CT misses subarachnoid hemorrhage 10% of the time. If CT is negative, a lumbar puncture is mandatory when subarachnoid hemorrhage is suspected.

D. Laboratory Studies

1. Blood glucose, electrolytes, BUN, creatinine, urinalysis; rapid plasma reagin (RPR) test to screen for syphilis.
2. **Complete Blood Count** may detect polycythemia or severe anemia. Platelet count, prothrombin time, and partial thromboplastin time may detect coagulopathies.
3. **Serum Thrombogenic Factors:** In younger patients with a history of miscarriages or deep vein thrombosis, anticardiolipoprotein, lupus anticoagulant, protein C, and protein S should be measured.

E. 12-lead ECG should be assessed for signs of concomitant myocardial infarction (ST elevation) or atrial fibrillation (a risk factor for stroke).

F. Plain chest films should exclude aspiration pneumonia. To evaluate swallowing ability.

G. Video fluoroscopic swallowing studies are indicated when the patient has a compromise in swallowing (eg, the patient coughs after drinking a small amount of water).

H. Echocardiography and Holter monitoring are recommended for evaluation of suspected cardiogenic embolism. Transesophageal echo should be obtained if transthoracic echo is negative, but a cardiogenic source if emboli is still suspected.

I. Carotid Ultrasonography with Doppler in the subacute phase should be considered if the patient has sustained a non-disabling, anterior circulation stroke or TIA and is a candidate for endarterectomy.

J. Electroencephalography is indicated if seizures have occurred. Up to 17% of stroke patients have early seizures.

IV. Differential Diagnosis of Stroke Syndromes

A. Large Vessel Thrombotic Event: Unilateral hemiparesis is consistent with a large vessel thrombotic event causing a contralateral hemispheric cortical infarction.

B. Lacunar Stroke

1. Characterized by focal hemiparesis without sensory loss, visual field cut, a language disorder in an elderly patient, pure sensory strokes,

or dysarthria with clumsiness of one hand.

2. Lacunar strokes are caused by small hemorrhages or infarcts of deep cerebral white matter, usually in hypertensive patients but also in those with diabetes or carotid atherosclerosis.

C. Cardiogenic Stroke is characterized by sudden onset of a maximal deficit, presence of a potential cardioembolic source (atrial fibrillation, myocardial infarction, patent foramen ovale, valvular disease, or severe heart failure), and the presence of multiple, bilateral, conical infarctions by CT. Evidence of embolism to other organs or echocardiographic thrombi may be apparent. 25% of all ischemic strokes are caused by cardioemboli.

D. Subacute Bacterial Endocarditis: Fever and a new cardiac murmur are suggestive of an embolism caused by endocarditis.

E. Arterial Dissection: Stroke following trauma to the head or neck raises the suspicion of a carotid or vertebral arterial dissection.

V. Immediate Management of Stroke

A. Airway and Breathing: First secure the ABCs--airway, breathing, and circulation. Maintain normal oxygenation and near-normal pCO_2. Labored or weak respirations are an indication for intubation and ventilation.

B. Hypertension may be either an initiating or a secondary event in stroke.

1. Blood pressure should not be aggressively reduced in ischemic stroke unless there is either severe hypertension (>220/120 mmHg), aortic dissection, heart failure or ischemia, hypertensive encephalopathy, or nephropathy. Overly aggressive blood pressure reduction reduces cerebral blood flow.
2. If treatment is needed, labetalol (Normodyne) is recommended. Reflex vasoconstriction and tachycardia are prevented by its alpha and beta blockade; 50 mg IV over 1 minute, repeated every 5 minutes if needed, or 2 mg/min IV infusion. Nitrates are contraindicated because they increase intracerebral pressure.
3. Nitroprusside may also be used; start the dosage at 0.25 mcg/kg/min IV, and increase at increments of 0.25 mcg/kg/min to a maximum of 10 mcg/kg/min.

C. Hyperglycemia: Existing diabetes can worsen after a stroke, and high blood glucose levels may increase tissue damage. Low doses of insulin should be administered if glucose >160 mg/dL. Intravenous fluid should be normal saline, not dextrose-saline.

D. Hyperthermia occurs in a third of stroke patients, and may increase brain damage. Acetaminophen and a cooling blanket may be necessary.

VI. Emergency Interventions in Stroke

A. Hemorrhagic Stroke

1. Immediate surgical evacuation may be required for aneurysm-induced hematomas, intracerebral hematomas, or cerebellar hematomas.
2. Surgery should not be delayed until the patient is lethargic or comatose.
3. **Elevated Intracranial Pressure**
   - **a.** May result from hemorrhage or from edema at about 24-48 hours. The most common initial sign is reduced level of consciousness.
   - **b.** Neurosurgical consultation for ventriculostomy should be obtained immediately.
   - **c.** Management consists of raising the head of the bed 30 degrees

and intubation and hyperventilation to lower pCO_2 to 25-30 mm Hg.

d. Mannitol: Loading dose of 25-50 g over 2-3 minutes; 25-g doses can be repeated if necessary, as often as every 4 hours.

e. Furosemide (Lasix): Indicated for overhydration, 20-40 mg IV.

f. Hypothermic cooling devices are used if hyperventilation and mannitol are unable to reduce intracranial pressure. Core body temperature is reduced to 94-96° F.

4. Subarachnoid Hemorrhage

a. Subarachnoid hemorrhage is the cause of 5% of strokes, and most are caused by a ruptured saccular aneurysm.

b. Immediate neurosurgical consultation and angiographic evaluation is necessary. Aneurysm clipping with clot removal will prevent rebleeding, lowering the rate of hydrocephalus and vasospasm.

c. Nimodipine (Nimotop), a semi-cerebroselective calcium channel blocker, should be administered to prevent vasospasm in subarachnoid hemorrhage; two 30-mg capsules q4h, beginning within 48 hours and continue for 21 days. Hypotension is common.

B. Ischemic Stroke

1. Antithrombotic therapy is given only if (1) the stroke is actively evolving, and the patient's condition is worsening; (2) TIAs are increasing in frequency and severity (crescendo TIAs); (3) high-grade vertebrobasilar atherothrombotic disease places the patient at risk for basilar artery occlusion; (4) arterial dissection; or (5) the stroke was caused by a cardiac embolus and is not massive.

a. Heparin: Begin at 700-800 u/hr (without a bolus). Maintain conservative prolongation of PTT (1.2-1.4 x control) as patients with cardioembolic stroke are at risk for cerebrovascular hemorrhage.

b. Warfarin (Coumadin): 5.0-7.5 mg PO qd x 3 days, then 2-4 mg qd. Maintain INR 2.0-2.5. Decrease if administered with amiodarone.

2. Avoid heparin if the patient is at risk for intraparenchymal bleeding, uncontrolled hypertension, or bleeding at another site.

3. Thrombolytics are considered only if hemorrhage has been excluded. Neurologic improvement may occur when initiated within 3 hours. t-PA: 0.9 mg/kg (max 90 mg) with 10% given as IV bolus, and remainder IV over 60 min.

VII. Continuing Treatment

A. Ischemic Stroke: When hemorrhage has been ruled out, consider treatments that prevent recurrent clot formation: Aspirin 325 mg/d is used. Ticlopidine, 250 mg PO bid, is appropriate for patients who cannot take aspirin, or who were already taking on aspirin at the time of stroke.

B. Lacunar Infarction should be treated with aspirin, 325 mg qd, and hypertension should be controlled.

C. Cardiogenic Embolism

1. With cardiogenic stroke, anticoagulation reduces the recurrence rate and is indicated if (1) there are no contraindications, (2) bleeding is not seen on brain imaging studies, (3) the infarct is not large, and (4) bacterial endocarditis is not a cause.

2. In patients with atrial fibrillation who cannot be given anticoagulants, aspirin reduces the stroke risk, but not by as much as warfarin.

D. General Care: Deep vein thrombosis is prevented with low-dose heparin and elastic stockings in patients with an immobile limb. After the

third day, small intracerebral hemorrhages do not contraindicate use of low doses of anticoagulants.

E. Nutrition: Nasogastric tube feeding is necessary if there is any compromise in swallowing. A soft diet with thickened liquids may be initiated later if tolerated.

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96 Stroke

Endocrinology and Nephrology

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Diabetic Ketoacidosis

I. Clinical Presentation

A. Diabetes is newly diagnosed in 20% of cases of diabetic ketoacidosis. The remainder of cases occur in known diabetics in whom ketosis develops after a precipitating factor, such as infection or noncompliance with insulin therapy.

B. Symptoms of DKA: Polyuria, polydipsia, fatigue, nausea, and vomiting developing over 1 to 2 days. Abdominal pain is prominent in 25%.

C. Physical Exam

1. Patients are typically flushed (despite hypotension) and tachycardiac. Tachypnea is common. Kussmaul's respiration, with deep breathing and air hunger, occurs when the serum pH is between 7.0 and 7.24.

2. A fruity odor on the breath indicates the presence of acetone, a by-product of diabetic ketoacidosis.

3. Fever is seldom present even though infection is common. Hypothermia may also occur.

4. Eighty percent of patients with diabetic ketoacidosis have altered mental status. Most are awake but confused; 10% are comatose.

D. Laboratory Findings

1. Serum glucose level >250 mg/dL

2. pH <7.35

3. Bicarbonate level below normal with an elevated anion gap

4. Presence of ketones in the serum

II. Differential Diagnosis

A. Diabetic ketoacidosis must be differentiated from other causes of ketosis, acidosis, and hyperglycemia.

B. Differential Diagnosis of Ketosis-Causing Conditions

1. Ketosis may result from alcoholic ketoacidosis or starvation.

2. The majority of patients with alcoholic ketoacidosis do not have diabetes, and the serum glucose level is not elevated. Alcoholic ketoacidosis occurs with heavy drinking and vomiting.

3. Starvation ketosis occurs after 24 hours without food and is not usually confused with diabetic ketoacidosis because glucose and serum pH are normal.

C. Differential Diagnosis of Acidosis-Causing Conditions

1. Metabolic acidoses are divided into increased anion gap (>14 mEq/L) and normal anion gap (anion gap is determined by subtracting the sum of chloride plus bicarbonate from sodium).

2. All ketoacidoses increase the anion gap (DKA, lactic acidosis, uremia, poisoning from salicylates or methanol).

3. Acidoses without an increased anion gap are associated with a normal glucose level and absent serum ketones. Non-anion gap

acidoses are caused by renal or gastrointestinal electrolyte losses.

D. Hyperglycemia Caused by Hyperosmolar Nonketotic Coma

1. Hyperosmolar coma occurs in patients with type II diabetes, and it causes severe hyperglycemia that must be distinguished from DKA. Patients are usually elderly and have a precipitating illness.
2. Serum glucose level is markedly elevated (>600 mg/dL), osmolarity is increased, and ketosis is minimal. Patients may be acidotic from lactic acidosis and renal failure resulting from dehydration.
3. Treatment of hyperosmolar, nonketotic coma consists of hydration and potassium replacement. Administration of insulin is less important and should be begun after fluid resuscitation is under way.

III. Treatment of Diabetic Ketoacidosis

A. Fluid Resuscitation

1. Fluid deficits average 5 L (50 to 100 mL/kg).
2. Give 1 liter of normal saline solution in the first hour and the second liter over the second and third hours. Thereafter, 1/2 normal saline solution should be infused at 250-500 mL/h.
3. Higher rates of fluid administration may be required in patients who are extremely dehydrated.
4. Lower rates are indicated for patients with chronic renal failure because they have not had major fluid losses.
5. When the glucose level reaches 250 mg/dL, 5% dextrose should be added to the replacement fluids to prevent hypoglycemia. If the glucose level declines rapidly, 10% dextrose should be used along with regular insulin IV infusion until ketosis resolves and anion gap normalizes.

B. Insulin

1. An insulin 0.1 U/kg IV bolus, followed by an infusion of 0.1 U/kg per hour is given. The biologic half life of IV insulin is less than 20 minutes, so an IV bolus without a follow-up infusion has a very short-lived effect, and serum glucose will rise rapidly if the insulin infusion is discontinued. Adjust the insulin infusion so that rate of glucose decline does not exceed 100 mg/dL per hour. Continue insulin infusion until anion gap normalizes.
2. When the bicarbonate level is greater than 16 mEq/L and the anion gap is less than 16 mEq/L, the insulin infusion rate should be decreased by half. However, if the bicarbonate level is not rising and the anion gap is not falling after 2 hours of treatment, the insulin infusion rate should be doubled.

C. Potassium

1. The most common preventable cause of death in patients with DKA is hypokalemia. Deficits are caused by osmotic diuresis and cellular shifts. The typical deficit is between 300 and 600 mEq.
2. Replacement therapy with potassium chloride should be started when fluid therapy is started. In most patients, the initial rate of potassium replacement is 20 mEq/h, but hypokalemia requires more aggressive replacement (40 mEq/h).
3. All patients should receive potassium replacement, except for those with known chronic renal failure, no urine output, or an initial serum potassium level greater than 6.0 mEq/L.

D. Sodium

1. Patients with diabetic ketoacidosis sometimes have a low serum

sodium level because the high level of glucose has a dilutional effect. For every 100 mg/dL that glucose is elevated, the sodium level should be assumed to be higher than the measured value by 1.6 mEq/L.

2. Frequently, patients have an initial serum sodium greater than 150 mEq/L, indicating severe dehydration. Initial rehydration fluid should consist of 1/2 normal saline.

E. Phosphate

1. Diabetic ketoacidosis depletes phosphate stores.
2. Serum phosphate level should be checked after 4 hours of treatment. If it is below 1.5 mg/dL, potassium phosphate or sodium phosphate should be added to the IV solution.

F. Bicarbonate

1. Administration of bicarbonate is ineffective in diabetic ketoacidosis, even in severely acidotic patients.
2. Bicarbonate administration may exacerbate hypokalemia and cause a paradoxic intracellular acidosis, a negative shift in the oxygen dissociation curve, and late alkalemia.

G. Additional Therapies

1. A nasogastric tube should be inserted in semiconscious patients to protect against aspiration.
2. Deep vein thrombosis prophylaxis should be provided for patients who are elderly, unconscious, or severely hyperosmolar; subcutaneous heparin, 5,000 U every 8 hours.

IV. Monitoring of Therapy

A. The serum bicarbonate level and anion gap should be monitored to determine the effectiveness of insulin therapy.

B. Follow-up evaluation of acidosis, not just of glucose level, is very important because in some patients glucose levels may normalize early in therapy, but the acidosis takes longer to resolve. Continued insulin infusion with a 10% glucose infusion may be needed to resolve the acidosis.

C. Glucose Levels: Check glucose level at 1-2 hour intervals during IV insulin administration

D. Electrolyte Levels: Assess q2h for first 6-8 hours, and then q4h

E. Phosphorus and magnesium levels should be checked after about 4 hours of treatment, and replacement therapy should be started if they are significantly below normal.

F. Testing for plasma and urine ketones is helpful in diagnosing diabetic ketoacidosis, but is not necessary during therapy.

V. Determining the Underlying Cause

A. Infection is the underlying cause of diabetic ketoacidosis in about 50% of cases. Infection of the urinary tract, skin, sinuses, or teeth should be sought. Fever is unusual in diabetic ketoacidosis and indicates infection when present; an elevated white blood cell count is usually present whether or not there is infection.

B. Physical examination, chest film, and urinalysis should be completed to exclude infection. If infection is suspected, antibiotics should be started empirically.

C. Omission of insulin doses (common in adolescents) is often a precipitating factor.

D. Myocardial infarction, ischemic stroke, and abdominal catastrophes

may precipitate DKA.

VI. Initiation of Subcutaneous Insulin

A. When the serum bicarbonate level is normal and the patient is ready to eat, subcutaneous insulin can be started.

B. It is critical to overlap intravenous and subcutaneous administration of insulin to avoid redevelopment of ketoacidosis. The intravenous infusion may be stopped 1 hour after the first subcutaneous injection of regular insulin.

C. Estimation of Subcutaneous Insulin Requirements

1. Multiply the final insulin infusion rate times 24 hours and divide the total into morning and evening doses.

2. Two thirds of the total dose is given in the morning, as two thirds NPH and one third regular insulin. The remaining one third of the total dose is given before supper as one half NPH and one half regular insulin.

3. Adjust subsequent doses according to the patient's blood glucose response.

VII. Complications

A. Death from diabetic ketoacidosis can be caused by hypokalemia, hypoglycemia, untreated infection, aspiration, thromboembolism, cerebral edema, and myocardial infarction.

B. Excessive use of normal saline solution can result in fluid overload and hypernatremia.

C. Cerebral edema occurs in 1 of 200 patients with diabetic ketoacidosis, usually in those younger than age 20. It is manifested by abrupt worsening of the mental status. Patients should be treated aggressively with dexamethasone and mannitol.

Renal Failure

I. Clinical Presentation of Acute Renal Failure

A. Acute renal failure is defined as a sudden decrease in renal function sufficient to increase the concentration of nitrogenous wastes in the blood, manifest by an increasing BUN or creatinine.

B. Oliguria is a common indicator of acute renal failure, and is marked by a decrease in urine output to less than 30 mL/h. Acute renal failure may be oliguric or nonoliguric (>30 mL/h). Anuria (<100 mL/day) is unusual, and its presence suggests obstruction or a vascular cause.

C. Acute renal failure may less commonly be manifest by encephalopathy, volume overload, pericarditis, bleeding, anemia, hyperkalemia, hyperphosphatemia, hypocalcemia, and metabolic acidemia.

II. Clinical Causes of Renal Failure

A. Prerenal Insult

1. Prerenal insult is the most common cause of acute renal failure, accounting for 70%. Prerenal failure is usually caused by reduced renal perfusion pressure secondary to extracellular fluid volume loss (diarrhea, diuresis, GI hemorrhage), or secondary to extracellular fluid sequestration (pancreatitis, sepsis), inadequate cardiac output, renal vasoconstriction (sepsis, liver disease, drugs), or inadequate fluid intake or replacement.

2. Most patients with prerenal azotemia have oliguria, a history of large fluid losses (vomiting, diarrhea, burns), and evidence of intravascular volume depletion (thirst, weight loss, orthostatic hypotension, tachycardia, flat neck veins, dry mucous membranes). Patients with congestive heart failure may have total body volume excess (distended neck veins, pulmonary and pedal edema) but still have compromised renal perfusion and prerenal azotemia because of diminished effective vascular volume and/or cardiac output.
3. The causes of prerenal failure are usually reversible if recognized and treated early; otherwise, prolonged renal hypoperfusion can lead to acute tubular necrosis and permanent renal insufficiency

B. Intrarenal Insult

1. Insult to the renal parenchyma (tubular necrosis) causes 20% of acute renal failure. Acute tubular necrosis is characterized by an abrupt decline in renal function caused by ischemic or toxic injury to the renal tubules.
2. Prolonged hypoperfusion is the most common cause of tubular necrosis.
3. Nephrotoxins (radiographic, aminoglycosides, contrast) are the second most common cause of tubular necrosis. Less common nephrotoxins include cisplatin, amphotericin, and pentamidine.
4. Pigmenturia induced renal injury can be caused by intravascular hemolysis or rhabdomyolysis.
5. Other causes of tubular necrosis include pyelonephritis, thrombosis, emboli, malignant hypertension, thrombotic thrombocytopenic purpura, hemolytic-uremic syndrome, and vasculitis.
6. Acute glomerulonephritis or acute inflammation of renal interstitium (acute interstitial nephritis) (usually from allergic reactions to beta-lactam antibiotics, sulfonamides, rifampin, NSAIDs, cimetidine, phenytoin, allopurinol, thiazides, furosemide, analgesics) are occasional causes of intrarenal kidney failure.

C. Postrenal Insult

1. Postrenal damage results from obstruction of urine flow. Postrenal insult is the least common of the three causes of acute renal failure, accounting for 10%.
2. Postrenal insult may be caused by extrarenal obstructive uropathy caused by prostate cancer, benign prostatic hypertrophy, or renal calculi occlusion of the bladder outlet.
3. Postrenal insult may be caused by intrarenal obstruction of the distal tubules by amyloidosis, uric acid crystals, multiple myeloma, or by drugs such as methotrexate and acyclovir.

III. Clinical Evaluation of Acute Renal Failure

A. Initial evaluation of renal failure should determine whether the cause is decreased renal perfusion, obstructed urine flow, or disorders involving the renal parenchyma. Review recent clinical events and drug therapy, including volume status (orthostatic pulse, blood pressure, fluid intake and output, daily weights, hemodynamic parameters), nephrotoxic medications, and pattern of urine output.

B. Prerenal azotemia is likely when there is a history of heart failure or extracellular fluid volume loss or depletion.

C. Postrenal azotemia is suggested by a history of decreased size or force of the urine stream, anuria, flank pain, hematuria or pyuria, or

cancer of the bladder, prostate, or pelvis. Anuria (complete absence of urine) usually results from obstructive uropathy; occasionally anuria indicates cessation of renal blood flow or rapidly progressive glomerulonephritis.

D. Acute tubular necrosis is suggested by a history of prolonged volume depletion (often post-surgical), pigmenturia, hemolysis, rhabdomyolysis, or nephrotoxins.

E. Intrarenal insult is suggested by recent radiocontrast, aminoglycoside use, or vascular catheterization. Glomerulonephritis may be implicated by a history of medication rash, fever, or arthralgias. Transient eosinophilia occurs in 80% of cases. Urinary studies may reveal hematuria, sterile pyuria, eosinophiluria, mild proteinuria (<2 g/24 h) and, rarely, white blood cell casts. NSAID-induced acute interstitial nephritis occurs most often with the use of ibuprofen, fenoprofen, and naproxen.

F. The presence of a disease known to cause chronic renal insufficiency (diabetes mellitus) may suggest chronic renal failure. The presence of normochromic normocytic anemia, hypercalcemia, and hyperphosphatemia also suggests chronic renal insufficiency.

IV. Physical Examination

A. Assess cardiac output, volume status, bladder size, and systemic disease manifestations.

B. Prerenal azotemia is suggested by impaired cardiac output (neck vein distention, pulmonary rales, pedal edema). Volume depletion is suggested by orthostatic blood pressure changes, weight loss, or low urine output.

C. Flank, suprapubic, or abdominal masses may indicate an obstructive cause.

D. Skin rash may suggests drug-induced interstitial nephritis; palpable purpura suggests vasculitis; nonpalpable purpura suggests thrombotic thrombocytopenic purpura or hemolytic-uremic syndrome--all of which are compatible with intrarenal kidney failure.

E. Bladder Catheterization is useful to rule out suspected bladder outlet obstruction; a residual volume of more than 100 mL suggests bladder outlet obstruction.

F. Central Venous Monitoring is used to measure cardiac output and left ventricular filling pressure if prerenal failure is suspected.

V. Laboratory Evaluation

A. Spot Urine Sodium Concentration

1. Spot urine sodium can help distinguish between prerenal azotemia and acute tubular necrosis.

2. Prerenal failure causes increased reabsorption of salt and water, and will manifest as a low spot urine sodium concentration <30 mEq/L and a low fractional sodium excretion <1%.
Fractional Excretion of Sodium (%) = ([urine sodium/plasma sodium] ÷ [urine creatinine/plasma creatinine] x 100)

3. If tubular necrosis is the cause, the spot urine concentration will be >50 mEq/L, and fractional excretion of sodium >1% because necrosed tubules do not efficiently reabsorb sodium. Urine spot sodium is non-diagnostic if loop diuretics have been used in the preceding 24 hours.

B. Urinalysis

1. Normal urine sediment is a strong indicator of prerenal azotemia or may be an indicator of obstructive uropathy.
2. Hematuria, pyuria, or crystals may be associated with postrenal obstructive azotemia.
3. Urine sediment containing abundant cells, casts, or proteins suggests an intrarenal disorder.
4. Red cells alone may indicate vascular disorders; RBC casts and abundant protein suggest glomerular disease (glomerulonephritis).
5. White cell casts and eosinophilic casts indicate interstitial nephritis.
6. Renal epithelial cell casts and pigmented granular casts are associated acute tubular necrosis.

C. Prerenal Failure is associated with hemoconcentration (increased albumin and hematocrit), elevated BUN and creatinine, and a BUN to creatinine ratio >20. Urinalysis may reveal a specific gravity greater than 1.015 but is otherwise unremarkable.

D. Ultrasound is useful for evaluation of suspected postrenal obstruction (nephrolithiasis) after bladder outlet obstruction has been ruled out by catheterization. Ultrasonography can be used to look above the bladder for dilated ureters. The presence of small (<10 cm in length), scarred kidneys is diagnostic of chronic renal insufficiency.

VI. Management of Acute Renal Failure

A. Rule out reversible disorders such as obstruction, and correct hypovolemia with adequate volume replacement, and maintain cardiac output to ensure adequate renal perfusion.

B. Extracellular Fluid Volume Expansion: Infusion of a 1-2 liter crystalloid fluid bolus may confirm suspected volume-depleted, prerenal azotemia.

C. In critically ill patients, physical examination and chest film are often inadequate guides to hemodynamic status. A pulmonary artery catheter should be used for monitoring.

D. If the patient remains oliguric despite euvolemia, consider measures to restore urine output with IV diuretics or renal vasodilators. Nonoliguric tubular necrosis is easier to manage than oliguric renal failure, and metabolic complications are less likely.

1. A large single dose of furosemide (200-300 mg) may be administered intravenously to promote diuresis. If urine flow is not improved, double the dose of furosemide, or give it in combination with metolazone (Zaroxolyn). Furosemide may be repeated in 2 hours or a continuous IV infusion of 10-40 mg/hr (max 1000 mg/day) may be used.
2. Mannitol 12.5-25 gm IV can also be effective, but it may worsen pulmonary edema if oliguria persists.
3. Urine flow may also be improved with low dose dopamine, 1-3 mcg/kg/min IV.

E. Modify either dosage or dosing intervals of renally excreted drugs, and monitor drug levels. Monitor blood count, electrolytes, creatinine, calcium, and phosphorus.

F. Hyperkalemia is the most immediately life-threatening complication. Serum potassium values greater than 6.5 mEq/L may lead to arrhythmias and cardiac arrest. Potassium should be removed from IV solutions, and potassium binding resins, orally or by enema, or urgent

dialysis may be required. Hyperkalemia may be treated with sodium polystyrene sulfonate (Kayexalate), 30-60 gm orally every 4-6 hours.

G. **Hyperphosphatemia** can be controlled with antacids containing calcium acetate, or aluminum compounds given with meals to bind dietary phosphorus. Antacids that contain magnesium are contraindicated.

H. **Metabolic Acidosis** can further aggravate hyperkalemia, alter cardiac function, and decrease pulmonary reserve. It is treated with oral sodium bicarbonate (Shohl's solution) to maintain the serum pH >7.2 and the bicarbonate level $\geq$18 mEq/L.

I. **Fluids:** After normal volume has been restarted, fluid intake should be reduced to an amount equal to urinary and other losses plus insensible losses of 300-500 mL/day. In oliguric patients, daily fluid intake may need to be restricted to less than 1 L.

J. **Nutritional Therapy:** Enteral nutrition is preferable to parenteral nutrition. A renal diet consisting of daily high biologic value protein intake of 0.8-1.0 g/kg, sodium 2 g, potassium 1 mEq/kg, and at least 35 kcal/kg of nonprotein calories can reduce hyperkalemia and azotemia without excessive catabolism.

K. **Dialysis:** Indications for dialysis include uremic pericarditis, severe hyperkalemia, pulmonary edema, persistent severe metabolic acidosis (pH less than 7.2), and symptomatic uremia.

Hyperkalemia

I. Pathophysiology of Potassium Homeostasis

A. 98% of body K is intracellular. Only 2% of total body potassium, about 70 mEq, is in the extracellular fluid where it is measured in serum at a normal concentration of 3.5-5 mEq/L.

B. The normal upper limit of plasma K is 5-5.5 mEq/L, with a mean K level of 4.3.

C. External Potassium Balance: Normal dietary K intake is 1-1.5 mEq/kg in the form of vegetables and meats. The kidney is the primary organ for preserving external K balance, excreting 90% of the daily K burden.

D. Internal potassium balance is defined as potassium transfer to and from tissues. Insulin, acid-base status, catecholamines, aldosterone, plasma osmolality, cellular necrosis, glucagon, and drugs affect internal potassium balance.

II. Clinical Disorders of External Potassium Balance

A. Chronic Renal Failure: The kidney is able to excrete the normal dietary intake of potassium until the glomerular filtration rate falls below 10 cc/minute, or until urine output falls below 1 L/day. Renal failure is advanced before hyperkalemia occurs.

B. Impaired Renal Tubular Function: Renal diseases may cause hyperkalemia. The renal tubular acidosis caused by these conditions may worsen hyperkalemia.

C. Primary Adrenal Insufficiency (Addison's disease)

1. Now a rare cause of hyperkalemia.
2. **Diagnosis** is indicated by the combination of hyperkalemia and hyponatremia, and is confirmed by a low aldosterone and a low

plasma cortisol level that does not respond to adrenocorticotropic hormone treatment.

3. **Treatment** requires glucocorticoid and mineralocorticoid agents and volume replacement with normal saline.

D. Drugs are among the most common causes of hyperkalemia including nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, cyclosporine, and potassium-sparing diuretics. Hyperkalemia is especially common when these drugs are given to patients at risk for hyperkalemia (diabetics, renal failure, hyporeninemic hypoaldosteronism, advanced age).

E. Excessive Potassium Intake

1. Long-term potassium supplementation results in hyperkalemia most often when an underlying impairment in renal excretion already exists.
2. Oral ingestion of 1 mEq/kg may increase the serum K level by 1 mEq/L an hour afterward in normal individuals. A single intravenous administration of 0.5 mEq/kg over 1 hour increases serum levels by a peak of 0.6 mEq/L. Hyperkalemia results when infusions of greater than 40 mEq/hour are given.
3. **Acute K Overload** may result from infusion from the dependent portion of an unmixed potassium solution or from ingestion of salt substitutes.

III. Clinical Disorders of Internal Potassium Balance

A. Diabetic patients are at particular risk for severe hyperkalemia because of renal insufficiency and hyporeninemic hypoaldosteronism.

B. Acidosis: Systemic acidosis reduces the excretion of potassium.

C. Endogenous potassium release from muscle injury, tumor lysis, or chemotherapy may elevate serum potassium.

IV. Manifestations of Hyperkalemia

A. Hyperkalemia, unless severe, is usually asymptomatic. The effect of hyperkalemia on the heart becomes significant above 6 mEq/L. As levels increase, the initial ECG change is tall peaked T waves, especially in the precordial leads. QT interval is normal or diminished.

B. As K levels rise further, the PR interval becomes prolonged, then the P wave amplitude decreases. QRS complexes widen into a sine wave pattern, representing a form of ventricular flutter, with subsequent cardiac standstill.

C. The electrocardiogram occasionally may display Q waves or ST elevation similar to myocardial infarction. Cardiac contractility is not impaired.

D. At serum K levels of 7 mEq/L, an ascending muscle weakness may lead to a flaccid paralysis that spares cranial nerve function. Sensory abnormalities, impaired speech, and respiratory arrest may follow.

V. Pseudohyperkalemia

A. Potassium may be falsely elevated by hemolysis during phlebotomy, when K is released from ischemic muscle distal to a tourniquet, and because of erythrocyte fragility disorders.

B. Falsely high laboratory measurement of serum potassium may occur in normokalemic subjects who have markedly elevated platelet (>10^6 platelet/mm^3) or white blood cell (>50,000/mm^3) counts.

VI. Diagnostic Approach to Hyperkalemia

A. The serum K level should be repeat tested to rule out laboratory error.

If significant thrombocytosis or leukocytosis is present, a plasma potassium level should be determined.

B. Renal and extrarenal causes of hyperkalemia should be distinguished as follows:

1. Measure 24 hour urine output, urinary K excretion, blood urea nitrogen, and serum creatinine.
2. Renal K retention is diagnosed when urinary K excretion is less than about 20 mEq/day while the serum K level is increased.
3. High urinary K and K excretion >20 mEq/day is indicative of excessive intake of K as the cause.

VII. Renal Hyperkalemia

A. If urinary K excretion is low and urine output is in the oliguric range and creatinine clearance is lower than about 20 cc/minute, renal failure is the probable cause. Prerenal azotemia resulting from volume depletion must be ruled out because the hyperkalemia will respond to volume restoration.

B. When urinary K excretion is low, yet blood urea nitrogen and creatinine levels are not elevated and urine volume is at least 1 L daily, and renal sodium excretion is adequate (about 20 mEq/day), then either a defect in the secretion of renin or aldosterone or a tubular resistance to aldosterone is likely. Low plasma renin and aldosterone levels, will confirm the diagnosis of hyporeninemic hypoaldosteronism. A specific cause of this entity should then be sought. If plasma aldosterone is low despite high renin values, the use of heparin should be suspected. Addison's disease and isolated hypoaldosteronism may occur and are diagnosed by serum aldosterone measurement.

C. When inadequate K excretion is not caused by hypoaldosteronism, a tubular defect in K clearance is suggested. Consider urinary tract obstruction, renal transplant, lupus, or a medication.

VIII. Extrarenal Hyperkalemia

A. When hyperkalemia occurs along with high urinary K excretion, >20 mEq/day, excessive intake of K is the cause. Potassium excess in IV fluids, diet, or medication should be sought. A concomitant underlying renal defect in K excretion is also likely to be present.

B. Measure blood sugar to rule out insulin deficiency; check blood pH and serum bicarbonate to rule out acidosis.

C. Rule out endogenous sources of K, such as tissue necrosis, hypercatabolism, hematoma, gastrointestinal bleeding, or intravascular hemolysis.

IX. Management of Hyperkalemia

A. The degree of elevation of serum K and severity of electrocardiographic changes determine the proper management of hyperkalemia.

B. Acute Treatment of Hyperkalemia

1. **Calcium Chloride**
   - **a.** Calcium chloride should be given IV if the electrocardiogram shows loss of P waves or widening of QRS complexes; calcium reduces the cell membrane threshold potential, but will not lower the potassium level.
   - **b.** 10% calcium gluconate should be given as 2-3 ampules over 5 minutes. In patients with circulatory compromise, give 1 ampule of calcium chloride IV over 3 minutes.
   - **c.** If the serum level of K is greater than 7 mEq/L, calcium should be

given because of imminent cardiac toxicity. If digitalis intoxication is suspected, calcium must be given cautiously. Coexisting hyponatremia should be treated with hypertonic saline.

2. **Insulin**
   - **a.** If the only ECG abnormalities are peaked T waves and the serum level is under 7 mEq/L, begin treatment with insulin (regular insulin, 5-10 U by IV push) with 50% dextrose water (D50W) 50 mLs IV push (unless the blood sugar is already substantially elevated).
   - **b.** Repeated insulin doses of 10 U can be given every 15 minutes for maximal effect, combined with glucose as needed.
3. **Sodium Bicarbonate**
   - **a.** Bicarbonate promotes cellular uptake of K, and it should be given as two 50-mEq ampules IV push. Bicarbonate is most effective when acidosis is present; however, alkalinization may be used even in the absence of low pH.
   - **b.** Avoid bicarbonate if severe heart failure or hypernatremia. If the serum calcium is low (as in uremic acidosis), calcium should also be given in a separate IV line to avoid hypocalcemic tetany during alkali therapy.
4. **Potassium Elimination Measures**
   - **a.** Furosemide (Lasix) 100 mg IV should be given immediately to promote kaliuresis; normal saline may be added to avoid volume depletion.
   - **b.** Sodium polystyrene sulfonate (Kayexalate) is a cation exchange resin that binds stool K. Give 30-60 gm with 50 cc of 20% sorbitol orally. A retention enema of 50-60 gm in 200 cc of 20% sorbitol has a more rapid effect.
   - **c.** Emergent hemodialysis specifically for hyperkalemia is not usually necessary, even in renal failure.

Hypokalemia

I. Pathophysiology of Hypokalemia

A. Hypokalemia is indicated by a serum K concentration of less than 3.5 mEq/L. Because 98% of K is intracellular.

B. Cellular Redistribution of Potassium: Hypokalemia may result from the intracellular shift of potassium by insulin (exogenous or glucose load), beta2 agonist drugs, stress induced catecholamine release, thyrotoxic periodic paralysis, alkalosis-induced shift (metabolic or respiratory), familial periodic paralysis, cellular proliferation (vitamin B12 treatment), hypothermia, and acute myeloid leukemia.

C. Nonrenal Potassium Loss

1. Gastrointestinal loss caused by diarrhea, laxative abuse, villous adenoma, biliary drainage, enteric fistula, clay ingestion, potassium binding resin ingestion or nasogastric suction.
2. Sweating, prolonged low potassium ingestion, hemodialysis and peritoneal dialysis may also account for nonrenal potassium loss.

D. Renal Potassium Loss

1. **Hypertensive High Renin States:** Malignant hypertension, renal

artery stenosis, renin-producing tumors.

2. **Hypertensive Low Renin, High Aldosterone States:** Primary hyperaldosteronism (adenoma or hyperplasia).
3. **Hypertensive Low Renin, Low Aldosterone States:** Congenital adrenal hyperplasia (11 or 17 hydroxylase deficiency), Cushing's syndrome or disease, exogenous mineralocorticoids (Florinef, licorice, chewing tobacco), Liddle's syndrome
4. **Normotensive**
   a. **Metabolic acidosis:** Renal tubular acidosis (type I or II)
   b. **Metabolic alkalosis (urine chloride <10 mEq/day):** Vomiting
   c. **Metabolic alkalosis (urine chloride >10 mEq/day):** Bartter's syndrome, diuretics, magnesium depletion, normotensive hyperaldosteronism
5. **Drugs** associated with potassium loss include amphotericin B, ticarcillin, piperacillin, loop diuretics.

II. Clinical Effects of Hypokalemia

A. Cardiac Effects

1. The most lethal consequence of hypokalemia is cardiac arrhythmias.
2. **Electrocardiographic Effects:** U waves >1 mm in height, T waves in the same lead; ST segment depression; T wave flattening, followed by inversion.
3. Atrial and ventricular ectopy, including ectopic atrial tachycardia, atrioventricular blocks, premature ventricular contractions, ventricular tachycardia and fibrillation. Arrhythmias of digitalis intoxication are worsened by hypokalemia and hypercalcemia.

B. Musculoskeletal Effects: The initial manifestation of K depletion is muscle weakness that can lead to paralysis. In severe cases, respiratory muscle paralysis may occur. Crampy pain, swelling, and paresthesias occur early.

C. Gastrointestinal Effects: Nausea, vomiting, constipation, and paralytic ileus may develop.

III. Diagnostic Evaluation

A. Determine 24-hour urinary potassium excretion.

B. If >20 mEq/day, excessive urinary K loss is the cause. If <20 mEq/d, low K intake, or nonurinary K loss is the cause.

C. In patients with excessive renal K loss and hypertension, measure plasma renin and aldosterone to differentiate adrenal from non-adrenal causes of hyperaldosteronism.

D. If hypertension is absent and patient is acidotic, renal tubular acidosis should be considered.

E. If hypertension is absent and serum pH is normal to alkalotic, a high urine chloride (>10 mEq/d) suggests hypokalemia secondary to diuretics or Bartter's syndrome. A low urine chloride (<10 mEq/d) suggests vomiting as a probable cause.

IV. Emergency Treatment of Hypokalemia

A. Estimated Potassium Deficit

1. At a serum K <3 mEq/L there is a K deficit of more than 300 mEq

2. At a serum K <2 mEq/L there is a K deficit of more than 700 mEq

B. Indications for Urgent Replacement: Electrocardiographic abnormalities consistent with severe K depletion, myocardial infarction, hypoxia, digitalis intoxication, marked muscle weakness, or respiratory muscle paralysis.

C. Intravenous Potassium Therapy

1. Intravenous KCL is usually used unless concomitant hypophosphatemia is present (diabetic ketoacidosis), where potassium phosphate is indicated. Intravenous K should be administered via a large peripheral or central vein.

2. Potassium chloride 20-40 mEq in 100 cc saline infused IVPB over 2 hours; or add up to 20-80 mEq to 1 liter of IV fluid and infuse over 2 hours; may combine with 40 mEq PO tid in addition to IV; total dose max is generally 100-200 mEq/d (3 mEq/kg/d).

3. Intravenous K infusions should be mixed in dextrose-free solutions because dextrose will stimulate endogenous insulin release, with subsequent K shift intracellularly.

4. The maximal rate of intravenous K replacement is 30 mEq/hour. The K concentration of IV fluids should be 40 mEq/L or less if given via peripheral vein.

5. Frequent monitoring of serum K and constant electrocardiographic monitoring are required when potassium is being infused.

D. If large doses of K fail to correct hypokalemia, or if diuretic-induced hypokalemia is present, determination of the serum magnesium level is indicated because magnesium levels less than 2 mg/dL will impair normalization of K.

V. Non-Emergent Therapy of Hypokalemia

A. Attempts should be made to normalize K levels if <3.5 mEq/L.

B. Oral supplementation is significantly safer than IV. Upper and lower gastrointestinal irritation, bleeding, and poor palatability are common. Micro-encapsulated and sustained-release forms of KCL are less likely to induce gastrointestinal disturbances than are wax-matrix tablets or liquid preparations.

1. KCL elixir, 1-3 tablespoon qd-tid PO after meals (20 mEq/Tbsp 10% sln).

2. Micro-K, 10 mEq tabs, 2-3 tabs tid PO after meals (40-100 mEq/d).

Hypomagnesemia

I. Pathophysiology

A. Hypomagnesemia is rare in healthy subjects because of the abundance of Mg in the food and water supply. Absorption of ingested Mg occurs in the small intestine. The kidneys regulate Mg balance.

B. Causes of Hypomagnesemia

1. Decreased Mg intake

2. Increased Mg losses

3. Alterations in the distribution of Mg

C. Decreased Magnesium Intake: Protein-calorie malnutrition is a common cause of hypomagnesemia. Inadequate caloric intake, prolonged parenteral (Mg-free) fluid administration, and catabolic illness also cause hypomagnesemia.

D. Gastrointestinal Losses of Magnesium: Gastrointestinal losses of Mg may result from prolonged nasogastric suction, laxative abuse, pancreatitis, extensive small bowel resection, short bowel syndromes, biliary and bowel fistulas, enteropathies, cholestatic liver disease, and malabsorption syndromes.

E. Renal Losses of Magnesium

1. Renal loss of Mg may occur secondary to renal tubular acidosis, glomerulonephritis, interstitial nephritis, or acute tubular necrosis.
2. Hyperthyroidism, hypercalcemia, and hypophosphatemia may cause Mg loss.
3. **Drugs Causing Mg loss:** Diuretic agents (furosemide, thiazides) induce hypomagnesemia by increasing Mg excretion. Digitalis, aminoglycoside antibiotics, cyclosporine, terbutaline, methotrexate, amphotericin, pentamidine, ethanol, and calcium are associated with hypomagnesemia.

F. Alterations in Magnesium Distribution

1. Redistribution of circulating Mg occurs by extracellular to intracellular shifts, chelation, sequestration, hungry bone syndrome, or by acute administration of glucose, insulin, or amino acids.
2. Mg depletion occurs during severe pancreatitis because of decreased intestinal absorption of Mg, prolonged nasogastric suction, administration of large quantities of parenteral fluids, and pancreatitis-induced sequestration of Mg.

II. Clinical Manifestations of Hypomagnesemia

A. Cardiovascular: Ventricular tachycardia, ventricular fibrillation, atrial fibrillation, multifocal atrial tachycardia, ventricular ectopic beats, hypertension, enhancement of digoxin-induced dysrhythmias, cardiomyopathies, and coronary artery spasm.

B. Neuromuscular and Behavioral: Convulsions, confusion, psychosis, weakness, ataxia, spasticity, tremors, tetany, agitation, delirium, and depression.

C. ECG changes: Prolonged PR and QT intervals, ST segment depression, T wave inversions, wide QRS complexes, tall T waves.

D. Concomitant Electrolyte Abnormalities of sodium, potassium, calcium, or phosphate are common.

III. Clinical Evaluation

A. Hypomagnesemia is diagnosed when the serum Mg concentration is less than 0.7-0.8 mMol/L, and symptomatic Mg deficiency occurs when the serum Mg concentration is less than 0.5 mMol/L.

B. Urinary Magnesium Determinations

1. 24-hour urine collection for magnesium is the first step in the evaluation of hypomagnesemia.
2. In hypomagnesemic states because of renal Mg loss, magnesium excretion exceeds 1.5-2.5 mMol/day.
3. Low urinary Mg excretion (<1 mMol/day) with concomitant serum hypomagnesemia, suggests Mg deficiency due to decreased intake, nonrenal losses, or redistribution of Mg.

IV. Treatment of Hypomagnesemia

A. Asymptomatic Magnesium Deficiency

1. In hospitalized patients, the daily Mg requirements can be provided through either a balanced diet, as oral Mg supplements (0.36-0.46 mEq/kg/day), or 16-30 mEq/day in a parenteral nutrition formulation.
2. Magnesium oxide tablets contain 111 mg (4.5 mMol, or 9 mEq) of elemental Mg. Magnesium oxide is better absorbed and less likely to cause diarrhea than magnesium sulfate.
3. Magnesium chloride (Slow-Mag) 65-130 mg (1-2 tabs) PO tid-qid (64 mg or 5.3 mEq/tab)

B. Symptomatic Magnesium Deficiency

1. Serum Mg 0.5 mMol/L or less, requires IV Mg repletion with electrocardiographic and respiratory monitoring.
2. 1-6 gm of magnesium sulfate in 500 mL of D5W is infused IV at 1 gm/hr. An additional 6-9 gms of $MgSO_4$ should be provided as intermittent bolus therapy or by continuous infusion over the next 24 hours. Parenteral $MgSO_4$ (4 mMol/g) is more frequently used than $MgCl_2$.
3. States of severe Mg deficiency may require additional therapy over a number of days because of slow repletion of cellular Mg stores.

Hypermagnesemia

I. Clinical Evaluation of Hypermagnesemia

A. Serum magnesium has a normal range of 0.8-1.2 mMol/L. Magnesium homeostasis is regulated by renal and gastrointestinal mechanisms.

B. Hypermagnesemia is usually iatrogenic and is frequently seen in conjunction with renal insufficiency.

C. Causes of Hypermagnesemia

1. **Renal:** Creatinine clearance <30 mL/minute.
2. **Nonrenal:** Excessive use of magnesium cathartics, especially with renal failure; iatrogenic overtreatment with magnesium sulfate.
3. **Combined Renal and Nonrenal:** Excessive magnesium in dialysates, iatrogenic overdosage of magnesium in patients with renal insufficiency.
4. **Less Common Causes of Mild Hypermagnesemia:** Hyperparathyroidism, Addison's disease, hypocalciuric hypercalcemia, lithium therapy.

D. Hypermagnesemia is commonly caused by overzealous replacement of presumed magnesium losses, inadequate adjustment of Mg dosage for renal insufficiency, and overuse of magnesium-containing cathartics.

E. Manifestations of Hypermagnesemia may include stupor and obtundation, respiratory failure, and cardiac arrhythmias. Hypermagnesemia should always be considered when these symptoms occur in patients with renal failure, in those receiving therapeutic magnesium, and in laxative abuse.

1. **Cardiovascular Manifestations**
   a. **Lower levels of hypermagnesemia <10 mEq/L:** Delayed interventricular conduction, first-degree heart block, prolongation of the Q-T interval.

b. Levels greater than 10 mEq/L: Heart block progressing to complete heart block and asystole occurs at levels greater than 12.5 mMol/L (>6.25 mMol/L).

c. Hypotension may occur but is usually only transient.

2. Neuromuscular Effects

a. Hyporeflexia occurs at a Mg level >4 mEq/L (>2 mMol/L); an early sign of magnesium toxicity is diminution of deep tendon reflexes caused by neuromuscular blockade.

b. Respiratory depression due to respiratory muscle paralysis occurs at levels >13 mEq/L (>6.5 mMol/L).

c. Somnolence and coma occur at very elevated levels.

II. Treatment of Hypermagnesemia

A. Asymptomatic, Hemodynamically Stable Patients

1. Moderate hypermagnesemia can be managed by elimination of intake and maintenance of renal magnesium clearance.

2. Saline diuresis and loop diuretics increase renal clearance of magnesium. Diuresis is adequate treatment if cardiovascular or respiratory compromise are absent.

B. Severe Hypermagnesemia

1. Severe hypermagnesemia requires loop diuretics, saline diuresis, and correction of acute cardiovascular or respiratory symptoms. Furosemide 20-40 mg IV q3-4h as needed. Frequently monitor input, output, and patient weight. Initiate saline diuresis with 0.9% or 0.45% saline infused at 150 cc/h to replace urine loss.

2. Calcium gluconate (10% sln; 1 gm per 10 mL amp) 1-3 ampules may be added to saline infusate to reverse acute cardiovascular toxicity and ameliorate respiratory failure. Calcium administration can be continued and given over a longer period of time (15 mg/kg, given as calcium gluconate over a 4-hour period) to increase renal excretion of magnesium.

C. If Renal Failure or Massive Overdose: Dialysis with magnesium-free dialysate is life-saving.

Disorders of Water and Sodium Balance

I. Pathophysiology of Water and Sodium Balance

A. Volitional intake of water is regulated by thirst.

B. Maintenance intake of water is the amount of water sufficient to offset obligatory losses.

Maintenance Water Needs:

= 100 mL/kg for first 10 kg of body weight
\+ 50 mL/kg for next 10 kg
\+ 20 mL/kg for weight greater than 20 kg

C. Clinical Signs of Hyponatremia: Confusion, agitation, lethargy, seizures, and coma. The rate of change during onset of hyponatremia is more important in causing symptoms than is the absolute concentration of sodium.

D. Pseudohyponatremia

1. A marked elevation of the blood glucose creates an osmotic gradient that pulls water from cells into the extracellular fluid, diluting the extracellular sodium. The contribution of hyperglycemia to hyponatremia can be estimated using the following formula:
   Expected change in serum sodium = (Serum glucose - 100) x 0.016
2. With normalization of the serum glucose level, the serum sodium level rises as a result of redistribution of body water.
3. Marked elevation of plasma solids (lipids or protein) can also result in erroneous hyponatremia because of laboratory inaccuracy. The percentage of plasma water can be estimated with the following formula:
   % plasma water = 100 - [0.01 x lipids (mg/dL)] - [0.73 x protein (g/dL)]

II. Diagnostic Evaluation of Hyponatremia

A. Exclude pseudohyponatremia by repeating testing, then determine the cause of the hyponatremia based on history, physical exam, urine osmolality, and urine sodium level. Determine if the patient is volume contracted, normal volume, or volume expanded.

B. Classification Hyponatremic Patients Based on Urine Osmolality

1. **Low Urine Osmolality (50-180 mOsm/L):** Indicates primary excessive water intake (psychogenic water drinking).
2. **High Urine Osmolality (urine osmolality >serum osmolality):**
   a. **High Urine Sodium (>40 mEq/L) and Volume Contracted:** Indicates a renal source of sodium and fluid loss (excessive diuretic use, salt-wasting nephropathy, Addison's disease, osmotic diuresis).
   b. **High Urine Sodium (>40 mEq/L) and Normal Volume:** Most likely because of water retention caused by a drug effect, hypothyroidism, or the syndrome of inappropriate antidiuretic hormone secretion (SIADH). In SIADH, the urine sodium level is usually high, but may be low if the patient is on a salt-restricted diet. SIADH is found in the presence of a malignant tumor or a disorder of the pulmonary or central nervous system.
   c. **Low Urine Sodium (<20 mEq/L) and Volume Contraction:** Dry mucous membranes, decreased skin turgor, and orthostatic hypotension indicate an extrarenal source of fluid loss (gastrointestinal disease, burns).
   d. **Low Urine Sodium (<20 mEq/L) and Volume-expanded, Edematous:** This disorder is caused by congestive heart failure, cirrhosis with ascites, and nephrotic syndrome; effective arterial blood volume is decreased. Decreased renal perfusion causes increased reabsorption of water.

III. Treatment of Water Excess Hyponatremia

A. Determine the Volume of Water Excess

Water excess = total body water x [(140/measured sodium) -1]

B. Treatment of Asymptomatic Hyponatremia: Restrict water intake to 1,000 mL/day. Food alone in the diet contains this much water, so no liquids should be consumed. If an intravenous solution is needed, an isotonic solution of 0.9% sodium chloride (normal saline) should be used. Dextrose should not be used in the infusion because the dextrose is metabolized into water.

C. Treatment of Symptomatic Hyponatremia

1. If neurologic symptoms of hyponatremia are present, the serum sodium level should be corrected with hypertonic saline. Excessively rapid correction of sodium may result in a syndrome of central pontine demyelination.
2. Raise the serum sodium at a rate of 1 mEq/L per hour. If chronic hyponatremia, limit the rate to 0.5 mEq/L per hour. Aim for a serum sodium of 125-130 mEq/L, then continue water restriction until the level normalizes.
3. The amount of hypertonic saline needed is estimated using the following formula:
   Sodium needed (mEq) = 0.6 x wt in kg x (desired sodium - measured sodium)
4. Hypertonic 3% sodium chloride contains 513 mEq/L of sodium. The calculated volume required should be administered over the period required to raise the serum sodium level at a rate of 0.5-1 mEq/L per hour.
5. Concomitant administration of furosemide may be required to lessen the risk of fluid overload, especially in the elderly.

IV. Hypernatremia

A. Clinical Manifestations of Hypernatremia

1. Signs of volume overload or volume depletion may be prominent.
2. Clinical manifestations include tremulousness, irritability, ataxia, spasticity, mental confusion, seizures, and coma. Symptoms are more likely to occur with acute increases in plasma sodium.

B. Causes of Hypernatremia

1. Net sodium gain, net water loss
2. Failure to replace obligate water losses, as in patients unable to obtain water because of an altered mental status or severe debilitating disease.
3. Diabetes Insipidus: If urine volume is high but urine osmolality is low, diabetes insipidus is the most likely cause.

V. Management of Hypernatremia

A. Acute treatment of hypovolemic hypernatremia depends on the degree of volume depletion.

1. If there is evidence of hemodynamic compromise (e.g., orthostatic hypotension, marked oliguria), fluid deficits should be corrected initially with isotonic saline.
2. Once hemodynamic stability is achieved, the remaining free water deficit should be corrected with 5% dextrose water or 0.45% NaCl.
3. The water deficit can be estimated using the following formula:
   Water deficit = 0.6 x wt in kg x [1 - (140/measured sodium)]

B. The change in sodium concentration should not exceed 1 mEq/liter/hour. Roughly one half of the calculated water deficit can be administered in the first 24 hours, followed by correction of the remaining deficit over the next 1-2 days. The serum sodium concentration and ECF volume status should be evaluated every 6 hours.

C. Excessively rapid correction of hypernatremia is dangerous as it may lead to lethargy and seizures secondary to cerebral edema.

D. Maintenance fluid needs from ongoing renal and insensible losses must also be provided. If the patient is conscious and able to drink, water should be given orally or by nasogastric tube.

VI. Mixed Disorders

A. Water Excess and Saline Deficit: Occurs when severe vomiting and diarrhea occur in a patient who is given only water; clinical signs of volume contraction and a low serum sodium are present. Saline deficit is replaced and free water intake is restricted until the serum sodium level has normalized.

B. Water and Saline Excess: Often occurs with heart failure with edema and a low serum sodium. An increase in the extracellular fluid volume, as evidenced by edema, is a saline excess. A marked excess of free water expands the extracellular fluid volume, causing apparent hyponatremia. However, the important derangement in edema is an excess of sodium. Sodium and water restriction and use of diuretics (furosemide) are usually indicated, in addition to treatment of the underlying disorder.

C. Water and Saline Deficit is frequently caused by vomiting and high fever, and is characterized by signs of volume contraction and an elevated serum sodium. Replace saline and free water in addition to maintenance amounts of water.

Hypophosphatemia

I. Clinical Manifestations: Heart failure, muscle weakness, tremor, ataxia, seizures, coma, respiratory failure, delayed weaning from ventilator, hemolysis, rhabdomyolysis.

II. Differential Diagnosis of Hypophosphatemia

A. Increased Urinary Excretion: Hyperparathyroidism, renal tubular defects, diuretics.

B. Decrease in GI absorption: Malnutrition, malabsorption, phosphate binding minerals (antacids).

C. Abnormal Vitamin D Metabolism: Vitamin D deficiency, familial hypophosphatemia, tumor-associated hypercalcemia.

D. Intracellular Shifts of Phosphate: Diabetic ketoacidosis, respiratory alkalosis, alcohol withdrawal, recovery phase of starvation.

III. Labs: Phosphate, SMA 12, LDH, Mg, Cal, albumin, PTH, urine electrolytes. 24h urine phosphate, and creatinine.

IV. Diagnostic Approach to Hypophosphatemia

A. 24 hr Urine Phosphate:

1. If 24 hour urine phosphate is less than 100 mg/day the causes include gastrointestinal losses (emesis, diarrhea, NG suction, phosphate binders), vitamin D deficit, refeeding, recovery from burns, alkalosis, alcoholism, DKA.

2. If 24 hour urine phosphate is greater than 100 mg/day, the causes include renal losses, hyperparathyroidism, hypomagnesemia, hypokalemia, acidosis, diuresis, renal tubular defects, and vitamin D deficiency.

V. Treatment

A. Mild Hypophosphatemia (1.0-2.5 mEq/dL)

1. Na or K phosphate 0.25 mMol/kg IV infusion at the rate of 10 mMoles/hr (in NS or D5W 150-250 mLs), may repeat as needed.

2. Neutral phosphate (Nutra-Phos), 2 capsules PO bid-tid (250 mg

elemental phosphorus/tab, 7 mEq Na+ & 7 mEq K+/tab) **OR**

3. Phospho-Soda (129 mg phosphorus, 4.8 mEq Na+/mL) 5 mL PO bid-tid.

B. Severe Hypophosphatemia (<1.0 mEq/dL)

1. Na or K phosphate 0.5 m Moles/Kg IV infusion at the rate of 10 mMoles/hr (NS or D5W 150-250 mLs), may repeat as needed.
2. Add potassium phosphate to IV solution in place of KCl (max 40 mEq/L infused at 100-150 mL/h). Max IV dose 7.5 mg phosphorus/kg/6-8h **OR** 2.5-5 mg elemental phosphorus/kg IV over 6-8h. Give as potassium or sodium phosphate (93 mg phosphate/mL and 4 mEq Na+ or K+/mL). Do not mix calcium and phosphorus in same IV.

Hyperphosphatemia

I. Clinical Manifestations of Hyperphosphatemia: Hypotension, bradycardia, arrhythmias, bronchospasm, apnea, laryngeal spasm, tetany, seizures, weakness, psychosis, confusion.

II. Clinical Evaluation of Hyperphosphatemia:

A. Exogenous Phosphate Administration: Enemas, laxatives, diphosphonates, vitamin D excess.

B. Endocrine Disturbances: Hypoparathyroidism (hypocalcemia will often cause hyperphosphatemia), acromegaly, PTH resistance.

C. Rule Out Excess Phosphate Production: Rhabdomyolysis, sepsis, fulminant hepatic failure, severe hypothermia, hemolysis, acidosis, renal failure, chemotherapy, tumor lysis syndrome.

D. Labs: Phosphate, SMA 12, Cal, parathyroid hormone. 24h urine phosphate, creatinine.

III. Therapy: Correct hypocalcemia, restrict dietary phosphate, saline diuresis.

A. Moderate Hyperphosphatemia:

1. Aluminum hydroxide (Amphojel) 5-10 mL or 1-2 tablets PO ac tid; aluminum containing agents bind to intestinal phosphate, and decreases absorption **OR**
2. Aluminum carbonate (Basaljel) 5-10 mL or 1-2 tablets PO ac tid **OR**
3. Calcium carbonate (Oscal) (250 or 500 mg elemental calcium/tab) 1-2 gm elemental calcium PO ac tid. Keep calcium-phosphate product <70; start only if phosphate <5.5.

B. Severe Hyperphosphatemia:

1. Volume expansion with 0.9% saline 1-3 L over 1-6h.
2. Acetazolamide (Diamox) 500 mg PO or IV q6h.
3. Consider dialysis.

References

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Commonly Used Formulas

A-a gradient = $[(P_B\text{-}PH_2O)\ FiO_2\text{-}PCO_2/R]\text{-}PO_2$ arterial

= (713 x FiO2-pCO2/0.8) -pO2 arterial

P_B = 760 mmHg; PH_2O = 47 mmHg ; R ≈ 0.8
normal Aa gradient <10-15 mmHg (room air)

Arterial O2 content = $1.36(Hgb)(Sa\ O_2)+0.003(Pa\ O_2)$

O2 delivery = CO x arterial O_2 content

Cardiac output = HR x stroke volume
Normal CO = 4-6 L/min

$$SVR = \frac{MAP\text{-}CVP}{CO_{L/min}} \times 80 = \text{NL } 800\text{-}1200 \text{ dyne/sec/cm}^2$$

$$PVR = \frac{PA\text{-}PCWP}{CO_{L/min}} \times 80 = \text{NL } 45\text{-}120 \text{ dyne/sec/cm}^2$$

Normal creatinine clearance = 100-125 ml/min(males), 85-105(females)

$$\text{Body water deficit (L)} = \frac{0.6(\text{weight kg})([\text{measured serum Na}]\text{-}140)}{140}$$

$$\text{Osmolality mOsm/kg} = 2[Na+ K] + \frac{BUN}{2.8} + \frac{glucose}{18} = \text{NL } 270\text{-}290 \ \frac{mOsm}{kg}$$

$$\text{Fractional excreted Na} = \frac{U\ Na/\ Serum\ Na \times 100}{U\ Cr/\ Serum\ Cr} = NL<1\%$$

Anion Gap = Na + K-(Cl + HCO3)

For each 100 mg/dl ↑ in glucose, Na+ ↓ by 1.6 mEq/L.

Corrected serum Ca^+ (mg/dl) = measured Ca mg/dl + 0.8 x (4-albumin g/dl)

Basal energy expenditure (BEE):
Males=66 + (13.7 x actual weight Kg) + (5 x height cm)-(6.8 x age)
Females= 655+(9.6 x actual weight Kg)+(1.7 x height cm)-(4.7 x age)

Nitrogen Balance = Gm protein intake/6.25-urine urea nitrogen-(3-4 gm/d insensible loss)

Commonly Used Drug Levels

DRUG	THERAPEUTIC RANGE*
Amikacin	Peak 25-30; trough <10 mcg/ml
Amiodarone	1.0-3.0 mcg/ml
Amitriptyline	100-250 ng/ml
Carbamazepine	4-10 mcg/ml
Clonazepam	20-80 NG/mL
Desipramine	150-300 ng/ml
Digoxin	0.8-2.0 ng/ml
Disopyramide	2-5 mcg/ml
Doxepin	75-200 ng/ml
Ethosuximide	40-100 mcg/ml
Flecainide	0.2-1.0 mcg/ml
Gentamicin	Peak 6.0-8.0; trough <2.0 mcg/ml
Imipramine	150-300 ng/ml
Lidocaine	2-5 mcg/ml
Lithium	0.5-1.4 meq/L
Mexiletine	1.0-2.0 mcg/ml
Nortriptyline	50-150 ng/ml
Phenobarbital	10-30 meq/ml
Phenytoin**	8-20 mcg/ml
Procainamide	4.0-8.0 mcg/ml
Quinidine	2.5-5.0 mcg/ml
Salicylate	15-25 mg/dl
Streptomycin	Peak 10-20; trough <5 mcg/ml
Theophylline	8-20 mcg/ml
Tocainide	4-10 mcg/ml
Valproic acid	50-100 mcg/ml
Vancomycin	Peak 30-40; trough <10 mcg/ml

* The therapeutic range of some drugs may vary depending on the reference lab used.

** Therapeutic range of phenytoin is 4-10 mcg/ml in presence of significant azotemia and/or hypoalbuminemia.

Index